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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS	3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS	4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS	5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS	6	Mar 08	Gene Names now available in BIOSIS
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NEWS	8	Mar 22	TRCTHERMO no longer available
NEWS	9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS	10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS	11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS	12	Apr 08	"Ask CAS" for self-help around the clock
NEWS	13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	14	Apr 09	ZDB will be removed from STN
NEWS	15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	19	Jun 03	New e-mail delivery for search results now available
NEWS	20	Jun 10	MEDLINE Reload
NEWS	21	Jun 10	PCTFULL has been reloaded
NEWS	22	Jul 02	FOREGE no longer contains STANDARDS file segment

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 10:25:53 ON 15 JUL 2002

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=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:26:03 ON 15 JUL 2002
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DICTIONARY FILE UPDATES:  14 JUL 2002  HIGHEST RN 438526-30-8

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
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Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09909797-1.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1               STR
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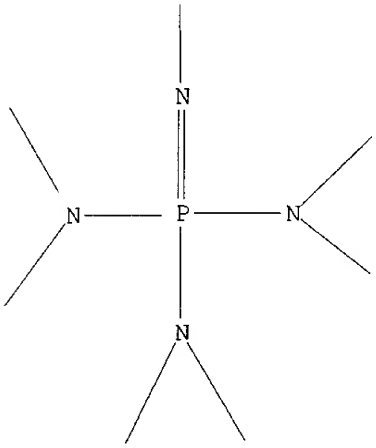


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Structure attributes must be viewed using STN Express query preparation.


=> s l1 exact sam
SAMPLE SEARCH INITIATED 10:27:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      2 TO ITERATE

100.0% PROCESSED       2 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            2 TO      124
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PROJECTED ANSWERS:                0 TO        0

L2             0 SEA EXA SAM L1

=> s l1 exact full
FULL SEARCH INITIATED 10:28:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     98 TO ITERATE

100.0% PROCESSED      98 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.03

L3             0 SEA EXA FUL L1

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      48.52      48.73

STN INTERNATIONAL LOGOFF AT 10:28:38 ON 15 JUL 2002


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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
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                   frequency
 NEWS  5  Feb 19   Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08   Gene Names now available in BIOSIS
 NEWS  7  Mar 22   TOXLIT no longer available
 NEWS  8  Mar 22   TRCTHERMO no longer available
 NEWS  9  Mar 28   US Provisional Priorities searched with P in CA/CAplus
                   and USPATFULL
 NEWS 10  Mar 28   LIPINSKI/CALC added for property searching in REGISTRY
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 NEWS 12  Apr 08   "Ask CAS" for self-help around the clock
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 NEWS 19  Jun 03  New e-mail delivery for search results now available
 NEWS 20  Jun 10  MEDLINE Reload
 NEWS 21  Jun 10  PCTFULL has been reloaded
 NEWS 22  Jul 02  FOREGE no longer contains STANDARDS file segment

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'CAPLUS' ENTERED AT 10:32:03 ON 15 JUL 2002
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FILE COVERS 1907 - 15 Jul 2002  VOL 137 ISS 3
FILE LAST UPDATED: 14 Jul 2002  (20020714/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> s heparin
```

```
         39238 HEPARIN
          1322 HEPARINS
L1       39304 HEPARIN
                (HEPARIN OR HEPARINS)

=> s l1 and depolymerization
          6435 DEPOLYMERIZATION
            27 DEPOLYMERIZATIONS
          6447 DEPOLYMERIZATION
                (DEPOLYMERIZATION OR DEPOLYMERIZATIONS)
          9302 DEPOLYMN
            36 DEPOLYMNS
          9314 DEPOLYMN
                (DEPOLYMN OR DEPOLYMNS)
         12535 DEPOLYMERIZATION
                (DEPOLYMERIZATION OR DEPOLYMN)
L2         256 L1 AND DEPOLYMERIZATION

=> s l2 and base
        539598 BASE
        126060 BASES
        618783 BASE
                (BASE OR BASES)
L3           7 L2 AND BASE

=> dis l3 1-7 ibib abs

L3   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:90113  CAPLUS
DOCUMENT NUMBER:          136:153008
TITLE:                    Heparin-derived polysaccharide mixtures,
                          preparation method and pharmaceutical compositions
                          containing same
INVENTOR(S):              Diaz, Jacques; Pecquet, Christelle; Perrin, Elisabeth;
                          Viskov, Christian
PATENT ASSIGNEE(S):       Aventis Pharma S.A., Fr.
SOURCE:                   PCT Int. Appl., 30 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     --------------    ----  --------       ---------------   --------
     WO 2002008295      A1   20020131       WO 2001-FR2332    20010718
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2811992         A1   20020125       FR 2000-9572      20000721
     US 2002055621      A1   20020509       US 2001-909797    20010723
PRIORITY APPLN. INFO.:                   FR 2000-9572      A  20000721
                                         US 2000-229123P   P  20000831
OTHER SOURCE(S):          MARPAT 136:153008
AB   The invention concerns heparin-derived polysaccharide mixts.
     having mol. wt. 1500-3000, anti-Xa activity 100-150 UI/mg, anti IIa
     activity 0-10 UI/mg, anti-Xa activity/anti-IIa activity >10, 2-26
     saccharide groups, 4,5-glucuronic 2-O-sulfate terminal groups, under
     alkali or alk.-earth metal salt form.  These mixts. are manufd. by
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depolymn. of quaternary ammonium salts of benzyl esters of **heparin** in org. solvent using a strong org. **base** having pKa >20 or Na imidazolate, transforming the resulting quaternary ammonium salt of the depolymd. benzylic ester to the Na salt, and sapon. of the ester.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:732851 CAPLUS
DOCUMENT NUMBER: 132:202459
TITLE: Structural characterization of low molecular weight **heparins**
AUTHOR(S): Casu, Benito; Torri, Giangiacomo
CORPORATE SOURCE: "G. Ronzoni" Institute for Chemical and Biochemical Research, Milan, 20133, Italy
SOURCE: Seminars in Thrombosis and Hemostasis (1999), 25(Suppl. 3), 17-25
CODEN: STHMBV; ISSN: 0094-6176
PUBLISHER: Thieme Medical Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 34 refs. Low mol. wt. **heparins** (LMWHs) obtained by different **depolymn**. processes can be distinguished from each other by characteristic end-residues, which are easily identified and quantified by nuclear-magnetic-resonance (NMR) spectroscopy. NMR spectroscopy characterizes major sulfation patterns as well as minor sequences such as the antithrombin-binding sequence and the linkage region of LMWHs. Artifacts assocd. with **base**-induced modifications such as the formation of iduronic acid epoxide and aziridine derivs. of N-sulfoglucosamine residues can also be detected. The influence of these modifications on the binding of **heparins** and LMWHs to proteins other than antithrombin are discussed.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:674055 CAPLUS
DOCUMENT NUMBER: 125:303695
TITLE: Preparation of saccharide oligomers by chemical **depolymerization** of **heparin** derivatives
INVENTOR(S): Vila Pahi, F. Javier; Farrerons Gallemt, Carles; Salvador Ravetllat, Luis; Gomis Torne, Pedro
PATENT ASSIGNEE(S): Bioiberica, S.A., Spain
SOURCE: Span., 11 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2077533	A1	19951116	ES 1994-395	19940228
ES 2077533	B1	19960701		

OTHER SOURCE(S): MARPAT 125:303695

AB The title oligomers, useful for prevention and treatment of thrombosis, are prepd. by (a) substituting carboxylic groups of a **heparin** salt (e.g., benzalkonium heparinate) with an anhydride mixt. having C1-4 alkyl or O-C1-4 alkyl terminals, (b) reacting with an org. **base** (e.g., Triton B) in an aprotic solvent to depolymerize, and (c) pptg. with a mixt. of NaCl soln., org. solvent, and water, and optionally (d) transforming the salt form to a acid form.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:410731 CAPLUS
DOCUMENT NUMBER: 119:10731
TITLE: Preparation of highly-sulfated **heparins** having improved antithrombotic activity
INVENTOR(S): Nagasawa, Kinzo; Uchama, Hideki
PATENT ASSIGNEE(S): Terumo Corp, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05032703	A2	19930209	JP 1991-210096	19910726

AB The title **heparins** are prepd. by heating the solid state or dispersion in a stabilized medium of salts between **heparin** and an arom. heterocyclic **base** to effect the intramol. migration of N-sulfate groups onto OH groups, and further sulfating the sulfate-depleted amino groups, followed by **depolymn**. of the substrate and/or fractionation to yield the low mol. wt. fractions. A **heparin**-pyridinium salt was prepd., desiccated with P2O5, heated 90 min at 90.degree., cooled, solubilized in water, sulfated, and depolymd.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:429293 CAPLUS
DOCUMENT NUMBER: 113:29293
TITLE: Polypeptide-carbohydrate conjugates with improved biological activity
INVENTOR(S): Lormeau, Jean Claude; Choay, Jean; Petitou, Maurice
PATENT ASSIGNEE(S): SANOFI, Fr.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 344068	A1	19891129	EP 1989-401421	19890524
EP 344068	B1	19930310		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2631970	A1	19891201	FR 1988-6892	19880524
FR 2631970	B1	19931224		
JP 02238879	A2	19900921	JP 1989-131227	19890524
AT 86632	E	19930315	AT 1989-401421	19890524
PRIORITY APPLN. INFO.:			FR 1988-6892	19880524
			EP 1989-401421	19890524

AB The pharmacodynamic and pharmacokinetic properties of polypeptides (e.g., tissue-type plasminogen activator, urokinase) are improved by conjugating the peptides with a glycosaminoglycan (e.g., **heparin**, dermatan sulfate). The sugar chain is grafted onto the polypeptide at a single point of the former, an aldehyde group that is either present normally or generated by **depolymn**. with HNO2. The poly-Schiff **base** resulting from the polypeptide-sugar reaction is reduced with cyanoborohydride to give the active product.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:50897 CAPLUS
DOCUMENT NUMBER: 112:50897
TITLE: Novel regio- and stereoselective modifications of

heparin in alkaline solution. Nuclear magnetic resonance spectroscopic evidence

AUTHOR(S): Jaseja, Mahesh; Rej, Rabindra N.; Sauriol, Francois; Perlin, Arthur S.

CORPORATE SOURCE: Dep. Chem., McGill Univ., Montreal, PQ, H3A 2A7, Can.

SOURCE: Can. J. Chem. (1989), 67(9), 1449-56
CODEN: CJCHAG; ISSN: 0008-4042

DOCUMENT TYPE: Journal

LANGUAGE: English

AB NMR spectroscopic evidence is presented in characterizing 3 new structurally modified forms of **heparin**. One of these, polymer M-I, represents a conversion of about two-thirds of the .alpha.-L-iduronic acid 2-sulfate residues (I) into residues of a 2,3-anhydro deriv. (II), through the action of NaOH. The formation of II is attributed to a **base**-catalyzed displacement of the sulfate group of I by an intramol. attack of O-3 on C-2. In more concd. NaOH soln., **heparin** is transformed almost quant. into polymer M-II, which differs from it in having residues of (nonsulfated) .alpha.-L-iduronic acid (III) in place of I. It is likely that II is an intermediate, and that a selective nucleophilic attack of hydroxide ion at C-2 accounts for the ido configuration in III. The third modification, giving polymer M-III, is induced when a neutral or weakly alk. soln. of M-I is heated at >70.degree., which promotes a different stereochem. in the hydrolysis of the 2,3-oxirane ring of II. Hence, in contrast to residues of III in M-II, most of the uronic acid residues of M-III appear to have the alternate, .alpha.-L-galacto, configuration. As shown by a comparison of beef lung and hog mucosal **heparin**, the rate at which M-I is converted into M-III is facilitated by the higher level of structural heterogeneity in the mucosal **heparin**. Whereas the formation of M-I, -II, and -III is accompanied by only moderate **depolymn**., these novel polymers retain little of the anti-coagulant and anti-XA activities of the unmodified **heparin**.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1969:54100 CAPLUS

DOCUMENT NUMBER: 70:54100

TITLE: Isolation and characterization of mucopolysaccharide fractions from animal tissues

AUTHOR(S): Fussi, Fernando; Colombo, U.; Fedeli, G. Franco

CORPORATE SOURCE: Lab. Biol. Zanoni, Milan, Italy

SOURCE: Boll. Chim. Farm. (1968), 107(11), 697-710
CODEN: BCFAAI

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In setting up methods for isolating and characterizing mucopolysaccharide (I) fractions from different animal tissues use was made of the soly. of the mucoproteins (II) in strong NaCl (6%) soln., selective protein sepn. by proteolytic enzymes and fullers earth, and complex formation between acid I and quaternary N **bases** (such as stearyl-benzyldimethylammonium chloride (III) and cetylpyridinium bromide (IV)). The fractionation, as exemplified with beef aorta, involved the sepn. of a fraction (A) sol. in 80% EtOH, the isolation of a mucopeptide (V) fraction (B) sol. in 10% CaCl2, splitting of the V by Lloyd's reagent, and the pptn. of the I moiety (fraction C) by NaCl. Submitting fraction C to autolysis and to **depolymn**. by hyaluronidase (VI) produced fractions D and E, resp. The I could also be isolated by employing III as pptg. agent, after fraction A was obtained, instead of resorting to the CaCl2 step, in which case fraction C1 was obtained. The latter fraction, dissolved in KCl 1.5M and fractionally pptd. in the presence of IV, yielded 3 subfractions pptg. at KCl 0.85, 0.4, and 0.15M, resp. The absence of ppt. above KCl 1M indicated the absence of **heparin**. The subfractions from KCl 0.85 and 0.15M were identified as chondroitin-4-sulfate (chondroitin sulfate A; (VII)) and chondroitin sulfate B (dermatan sulfate; (VIII), supported by examns. of their electrophoretic mobility and specific optical rotation, with yields of 44

and 39%, resp., of the total Cl obtained. The identity of VII with the 0.85M KCl fraction was further supported by the disappearance of the fractions with equal electrophoretic mobilities after hydrolysis with VI. The 2 components detected in the subfraction from 0.4M KCl were tentatively identified as keratan sulfate and heparitin sulfate (IX), with yields of 9.5 and 7.5% of the total Cl obtained. Procedures for the isolation of I from beef tracheal and nasal cartilages, and for obtaining hyaluronic acid (X) from human umbilical cord were also described. The procedures employed gave fractions with compns. as follows: (1) aorta: fraction A (EtOH-sol. ext.) peptides 45 and ash 52%; fraction B (II fraction) VII 6, VIII/IX 4, proteins 55, and ash 37%; fraction C (I fraction) VII 56.5, VIII 11, IX 7.5, protein and peptides <1%, and X absent; (2) tracheal and nasal cartilages: VII 75-80%, chondroitin-6-sulfate (chondroitin sulfate C; (XI)) in traces, and peptides and neutral glycoproteins (XII) present; (3) umbilical cord VIII/IX 3 and X 87%. The depolymd. I from aorta (fraction E) was present as a minor component in the II (fraction B) and in the I from aorta (fractions C and C1), and also in traces in X from umbilical cord. VII was practically the only constituent of the I from tracheal and nasal cartilages in which the I differed in the degree of polymn. XI was perhaps a minor constituent of X (where it was not clearly distinguishable from eventual VIII) and of I from aorta. The I from tracheal and nasal cartilages may also have contained neutral XII as impurities.

```
=> s l2 and phosphazene
          4125 PHOSPHAZENE
          1225 PHOSPHAZENES
          4464 PHOSPHAZENE
                 (PHOSPHAZENE OR PHOSPHAZENES)
L4           1 L2 AND PHOSPHAZENE

=> dis l4 bib abs

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:90113  CAPLUS
DN   136:153008
TI   Heparin-derived polysaccharide mixtures, preparation method and
     pharmaceutical compositions containing same
IN   Diaz, Jacques; Pecquet, Christelle; Perrin, Elisabeth; Viskov, Christian
PA   Aventis Pharma S.A., Fr.
SO   PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 2002008295      A1    20020131      WO 2001-FR2332   20010718
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2811992          A1    20020125      FR 2000-9572     20000721
     US 2002055621       A1    20020509      US 2001-909797   20010723
PRAI FR 2000-9572        A     20000721
     US 2000-229123P     P     20000831
OS   MARPAT 136:153008
AB   The invention concerns heparin-derived polysaccharide mixts.
     having mol. wt. 1500-3000, anti-Xa activity 100-150 UI/mg, anti IIa
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activity 0-10 UI/mg, anti-Xa activity/anti-IIa activity >10, 2-26 saccharide groups, 4,5-glucuronic 2-O-sulfate terminal groups, under alkali or alk.-earth metal salt form. These mixts. are manufd. by **depolymn**. of quaternary ammonium salts of benzyl esters of **heparin** in org. solvent using a strong org. base having pKa >20 or Na imidazolate, transforming the resulting quaternary ammonium salt of the depolymd. benzylic ester to the Na salt, and sapon. of the ester.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l2 and guanidine
         23529 GUANIDINE
          2604 GUANIDINES
         24501 GUANIDINE
                 (GUANIDINE OR GUANIDINES)
L5           0 L2 AND GUANIDINE

=> s l2 and guanine
         52446 GUANINE
          1024 GUANINES
         52835 GUANINE
                 (GUANINE OR GUANINES)
L6           0 L2 AND GUANINE

=> s l2 and imidazolate
           503 IMIDAZOLATE
            28 IMIDAZOLATES
           510 IMIDAZOLATE
                 (IMIDAZOLATE OR IMIDAZOLATES)
L7           1 L2 AND IMIDAZOLATE

=> dis l7 bib abs

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:90113  CAPLUS
DN   136:153008
TI   Heparin-derived polysaccharide mixtures, preparation method and
     pharmaceutical compositions containing same
IN   Diaz, Jacques; Pecquet, Christelle; Perrin, Elisabeth; Viskov, Christian
PA   Aventis Pharma S.A., Fr.
SO   PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.          KIND  DATE          APPLICATION NO.  DATE
     ------------------  ----  --------      ---------------  --------
PI   WO 2002008295       A1    20020131      WO 2001-FR2332   20010718
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2811992          A1    20020125      FR 2000-9572     20000721
     US 2002055621       A1    20020509      US 2001-909797   20010723
PRAI FR 2000-9572        A     20000721
     US 2000-229123P     P     20000831
OS   MARPAT 136:153008
AB   The invention concerns heparin-derived polysaccharide mixts.
     having mol. wt. 1500-3000, anti-Xa activity 100-150 UI/mg, anti IIa
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activity 0-10 UI/mg, anti-Xa activity/anti-IIa activity >10, 2-26 saccharide groups, 4,5-glucuronic 2-O-sulfate terminal groups, under alkali or alk.-earth metal salt form. These mixts. are manufd. by **depolymn.** of quaternary ammonium salts of benzyl esters of **heparin** in org. solvent using a strong org. base having pKa >20 or Na **imidazolate**, transforming the resulting quaternary ammonium salt of the depolymd. benzylic ester to the Na salt, and sapon. of the ester.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l2 and peroxide
        157827 PEROXIDE
         37595 PEROXIDES
        173297 PEROXIDE
                (PEROXIDE OR PEROXIDES)
L8            7 L2 AND PEROXIDE

=> s l8 and hydrogen
        683531 HYDROGEN
          4917 HYDROGENS
        686390 HYDROGEN
                (HYDROGEN OR HYDROGENS)
L9            5 L8 AND HYDROGEN

=> dis l9 1-5 bib abs
```

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2002:220927 CAPLUS
DN 136:252468
TI Methods and products related to low molecular weight **heparin**
IN Sundaram, Mallikarjum; Venkataraman, Ganesh; Shriver, Zachary; Liu, Dongfang; Qi, Yi Wei; Sasisekharan, Ram
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002023190	A2	20020321	WO 2001-US28457	20010912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-231994P P 20000912
AB The invention relates to methods and products for characterizing and using polysaccharides. Low mol. wt. **heparin** products and methods of use are described. Methods for characterizing purity and activity of polysaccharide prepns. including glycosaminoglycans such as **heparin** are also described. Heparinase was used for the cleavage of antithrombin III binding site in **heparin** and prodn. of low mol. wt. **heparin**.

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:405217 CAPLUS
DN 136:221578
TI **Depolymerization** of **heparin** and preparation of low

molecular weight **heparin**
AU Zhang, Wanzhong; Wang, Yunshan; Ma, Runyu; Su, Zhiguo
CS Department of Biochemical, Beijing University of Chemical Technology, Beijing, 100029, Peop. Rep. China
SO Zhongguo Shenghua Yaowu Zazhi (2001), 22(1), 48-51
CODEN: ZSYZFP; ISSN: 1005-1678
PB Zhongguo Shenghua Yaowu Zazhi Bianjibu
DT Journal
LA Chinese
AB The **depolymn.** of **heparin** and prepn. of low mol. wt. **heparin** were studied. The methods for **depolymn.** of **heparin** with nitrous acid, beta elimination, **hydrogen peroxide**, periodic acid, sulfuric acid-chloro-sulfonic acid, hypo-chloric acid and enzymes were studied and compared. The methods of prepns. of low mol. wt. **heparin** were also compared.

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1999:312745 CAPLUS
DN 130:326511
TI Manufacture of uniform low-molecular weight **heparin** by **depolymerization** of **heparin**
IN Hoshi, Yasuo
PA Shimizu Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 11130801	A2	19990518	JP 1997-296969	19971029

AB Low-mol. wt. **heparin** having (anti-factor Xa activity)/(antithrombotic activity) ratio 1.5-3.0 is manufd. by reacting Z parts **heparin** with X parts **peroxides** in the presence of divalent metal salts at 60-80.degree. for 3-8 h, wherein X and Z satisfy the following equation; X = Y/100 .times. Z .times. W [Y = content (%) of sulfate-substituted uronic acid groups in the **heparin**; W = 0.04-1]. Low-mol. wt. **heparin** is known as an antithrombotic agent which very rarely causes bleeding. A soln. of **heparin** was reacted with aq. H2O2 in the presence of Cu(OAc)2 at 70-75.degree. for 30 min to give 63% **heparin** with av. mol. wt. 5800 and (anti-factor Xa activity)/(antithrombotic activity) ratio 1.9. The ratio remained the same when stored at 40.degree. for 6 mo.

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1989:121368 CAPLUS
DN 110:121368
TI **Depolymerization** of natural polyanions, such as nucleic acids and glycosaminoglycans
PA Ajorca S. A., Argent.
SO Belg., 10 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 1000118	A6	19880405	BE 1987-861	19870804
	ES 2007373	A6	19890616	ES 1987-2175	19870724
	CH 678326	A	19910830	CH 1987-2953	19870731
	SU 1639432	A3	19910330	SU 1987-4203197	19870803
	CN 87105497	A	19880413	CN 1987-105497	19870805
PRAI	AR 1986-304799		19860805		

AB The title process is carried out with H2O2, in the presence of Fe(II) salts, by a process involving formation of free radicals. **Heparin**

Na (20 g) in 100 mL water was treated with 4 g Amberlite IR-120 (H+) followed by filtration. The filtrate (pH 4-4.5) was heated at 80.degree., with 4 mL 30% H2O2 and 0.2 mL Fe(II) compd. soln. (1.5 g FeSO4.7H2O in 100 mL water). After 1 h the reaction was stopped with EtOH. The av. mol. wt. of the depolymd. **heparin** Na was 4.000, as compared to 12,000 for the starting product.

L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1987:478204 CAPLUS
DN 107:78204
TI Depolymerized hexosaminoglucan sulfates with antithrombotic, fibrinolytic, and antiinflammatory activity
IN Mascellani, Giuseppe; Bianchini, Pietro
PA Opocrin S.p.A., Italy
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8606729	A1	19861120	WO 1986-EP291	19860515
	W: AU, DK, HU, JP, NO, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	DD 251355	A5	19871111	DD 1986-290192	19860513
	IL 78772	A1	19910816	IL 1986-78772	19860513
	AU 8659533	A1	19861204	AU 1986-59533	19860515
	AU 601910	B2	19900920		
	EP 221977	A1	19870520	EP 1986-903331	19860515
	EP 221977	B1	19900808		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 63500184	T2	19880121	JP 1986-503130	19860515
	JP 2510177	B2	19960626		
	HU 46028	A2	19880928	HU 1986-3344	19860515
	HU 203565	B	19910828		
	AT 55396	E	19900815	AT 1986-903331	19860515
	ZA 8603651	A	19870128	ZA 1986-3651	19860516
	CA 1283098	A1	19910416	CA 1986-509396	19860516
	CN 86104301	A	19870304	CN 1986-104301	19860517
	CN 1009096	B	19900808		
	DK 8700157	A	19870113	DK 1987-157	19870113
	DK 173804	B1	20011105		
	US 4973580	A	19901127	US 1989-349706	19890510
PRAI	IT 1985-20769	A	19850517		
	EP 1986-903331	A	19860515		
	WO 1986-EP291	A	19860515		
	US 1987-6497	B1	19870109		

AB The title polysaccharides were prepd. by a free radical-initiated **depolymn.** of natural polysaccharides, such as **heparins**, heparan sulfates, dermatan sulfates, chondroitin sulfates, and hyaluronic acid in aq. soln. at 20-70.degree. using a **peroxide** selected from the group consisting of AcOOH, 3-ClC6H4C(O)OOH, H2O2, cumene hydroperoxide, Na2S2O8, and BzOOH, and a catalyst selected from Cu2+, Fe2+, Cr3+ and Cr2O72-. They are useful as antithrombotic, fibrinolytic and antiinflammatory agents with poor or no anticoagulant activity. Thus, 9% aq. H2O2 was added with stirring at 35-60.degree. in 2.5 h to a soln. of 1 kg HFA 15 raw **heparin**, 0.495 kg NaCl, and 1 kg AcONa in 10 L H2O contg. 0.46 g Cu(OAc)2.H2O while holding the pH at 7.5 by addn. of 1N NaOH. The mixt. was successively treated with EDTA, AcOH, and MeOH to give a ppt. which was redissolved in H2O and again treated as described above to give 845.5 g **heparin** with mol. wt. of 4600. This showed activated anti-factor X activity in vitro.

=> s thrombosis

```
L10      14757 THROMBOSIS

=> s l10 and venous
         29698 VENOUS
L11       2737 L10 AND VENOUS

=> s l11 and treat
         41211 TREAT
          6254 TREATS
         47182 TREAT
                 (TREAT OR TREATS)
L12         36 L11 AND TREAT

=> s l12 and heparin
         39238 HEPARIN
          1322 HEPARINS
         39304 HEPARIN
                 (HEPARIN OR HEPARINS)
L13         19 L12 AND HEPARIN

=> dis l13 1-19 bib abs

L13  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:335897  CAPLUS
TI   How we diagnose and treat deep vein thrombosis
AU   Hirsh, Jack; Lee, Agnes Y. Y.
CS   Henderson Research Centre, and the Department of Medicine, McMaster
     University, Hamilton, ON, Can.
SO   Blood (2002), 99(9), 3102-3110
     CODEN: BLOOAW; ISSN: 0006-4971
PB   American Society of Hematology
DT   Journal
LA   English
AB   Making a diagnosis of deep vein thrombosis (DVT) requires both
     clin. assessment and objective testing because the clin. features are
     nonspecific and investigations can be either falsely pos. or neg.  The
     initial step in the diagnostic process is to stratify patients into high-,
     intermediate-, or low-risk categories using a validated clin. model.  When
     the clin. probability is intermediate or high and the venous
     ultrasound result is pos., acute symptomatic DVT is confirmed.  Similarly,
     when the probability is low and the ultrasound result is normal, DVT is
     ruled out.  A low clin. probability combined with a neg. D-dimer result
     can also be used to rule out DVT, thereby obviating the need for
     ultrasonog.  In contrast, when the clin. assessment is discordant with the
     results of objective testing, serial venous ultrasonog. or
     venog. is required to confirm or refute a diagnosis of DVT.  Once a
     patient is diagnosed with an acute DVT, low-mol.-wt. heparin
     (LMWH) is the agent of choice for initial therapy and oral anticoagulant
     therapy is the std. for long-term secondary prophylaxis.  Therapy should
     continue for at least 3 mo; the decision to continue treatment beyond 3 mo
     is made by weighing the risks of recurrent thrombosis and
     anticoagulant-related bleeding, and is influenced by patient preference.
     Screening for assocd. thrombophilia is not indicated routinely, but should
     be performed in selected patients whose clin. features suggest an
     underlying hypercoagulable state.  Several new anticoagulants with theor.
     advantages over existing agents are undergoing evaluation in phase 3
     studies in patients with venous thromboembolism.
RE.CNT  55    THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13  ANSWER 2 OF 19  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:219455  CAPLUS
DN   136:350368
TI   Randomized trial of different regimens of heparins and in vivo
     thrombin generation in acute deep vein thrombosis
```

AU Kakkar, Vijay V.; Hoppenstead, Debra A.; Fareed, Jawed; Kadziola, Zbigniew; Scully, Mike; Nakov, Roumen; Breddin, Hans K.
CS Thrombosis Research Institute, London, SW3 6LR, UK
SO Blood (2002), 99(6), 1965-1970
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Low-mol.-wt. and unfractionated **heparins** are frequently used to **treat venous** thromboembolism, but it is not known whether they are equally effective in inhibiting in vivo generation of thrombin. In this multicenter trial, 1048 patients were randomized to i.v. unfractionated **heparin** (group A), twice daily low-mol.-wt. **heparin** (reviparin) for 1 wk (group B), or once daily reviparin for 4 wk (group C). All patients received vitamin K antagonists. Blood samples withdrawn at the baseline and at weeks 1 and 3 were analyzed using markers of in vivo thrombin generation and other coagulation parameters. During the first 3 wk symptomatic recurrent deep vein **thrombosis** -pulmonary embolism (DVT/PE) occurred in 17 (4.5%) of 375 patients in group A compared with 4 (1.0%) of 388 patients in group B, and 9 (2.4%) of 374 patients in group C. Forty percent of patients in group A, 53.4% in group B, and 53.5% in group C showed 30% or greater redn. in thrombus size assessed by venog. Patients in group B had significantly greater redn. in D-dimer, prothrombin fragments 1 and 2 (F1+2), endogenous thrombin potential (ETP), and thrombin-antithrombin (TAT) complexes compared to groups A and C. Greater release of tissue factor pathway inhibitor (TFPI) and redn. in levels of thrombin activatable fibrinolysis inhibitor (TAFI) and fibrinogen were significantly more pronounced in group C patients. Reviparin administered twice daily plus vitamin K antagonist is more effective in inhibiting in vivo thrombin generation compared to i.v. unfractionated **heparin** plus vitamin K antagonist, and reviparin once daily produced significantly higher TFPI release and greater redn. in TAFI and fibrinogen levels.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 2001:196406 CAPLUS
DN 135:174958
TI Effects of a low-molecular-weight **heparin** on thrombus regression and recurrent thromboembolism in patients with deep-vein **thrombosis**
AU Breddin, Hans Klaus; Hach-Wunderle, Viola; Nakov, Roumen; Kakkar, Vijay V.
CS International Institute of Thrombosis and Vascular Diseases, Frankfurt, Germany
SO New England Journal of Medicine (2001), 344(9), 626-631
CODEN: NEJMAG; ISSN: 0028-4793
PB Massachusetts Medical Society
DT Journal
LA English
AB Background: Low-mol.-wt. **heparins** are frequently used to **treat venous** thromboembolism, but optimal dosing regimens and clin. outcomes need further definition. Methods: In this multicenter, open-label study with blinded adjudication of end points, we randomly assigned patients with acute deep-vein **thrombosis** to one of three treatment regimens: i.v. administration of unfractionated **heparin**; s.c. administration of a low-mol.-wt. **heparin**, reviparin, twice a day for one week; or s.c. administration of reviparin once a day for four weeks. The primary end point was evidence of regression of the thrombus on venog. on day 21; secondary end points were recurrent **venous** thromboembolism, major bleeding within 90 days after enrollment, and death. Results: Of the patients receiving unfractionated **heparin**, 40.2 % (129 of 321) had thrombus regression, as compared with 53.4 % (175 of 328) of the patients receiving reviparin twice daily and 53.5 % (167 of 312) of the patients receiving

reviparin once daily. With regard to thrombus regression, reviparin administered twice daily was significantly more effective than unfractionated **heparin** (relative likelihood of thrombus regression, 1.28; 97.5 % confidence interval, 1.08 to 1.52), as was reviparin administered once daily (relative likelihood, 1.29; 97.5 % confidence interval, 1.08 to 1.53). Mortality and the frequency of episodes of major bleeding were similar in the three groups. Conclusions: In acute deep-vein **thrombosis**, reviparin regimens are more effective than unfractionated **heparin** in reducing the size of the thrombus. Reviparin is also more effective than unfractionated **heparin** for the prevention of recurrent thromboembolism and equally safe.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 2000:867645 CAPLUS
DN 135:70905
TI Utilization and outcomes of enoxaparin treatment for deep-vein **thrombosis** in a tertiary-care hospital
AU Gilbert, Kristine B.; Rodgers, George M.
CS Office of Performance Monitoring and Improvement, The University of Utah Health Sciences Center, Salt Lake City, UT, 84132, USA
SO American Journal of Hematology (2000), 65(4), 285-288
CODEN: AJHEDD; ISSN: 0361-8609
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The availability of a low-mol.-wt. **heparin**, enoxaparin, to **treat** deep-vein **thrombosis** (DVT) offers the option for outpatient therapy for certain DVT patients. We monitored the utilization and outcomes of enoxaparin treatment for DVT in our tertiary-care hospital. A retrospective chart survey was performed for all DVT patients treated at our facility between Oct. 1998 and Sept. 1999. We tracked treatment received (unfractionated **heparin** or enoxaparin), clin. outcomes (recurrent thromboembolism or bleeding), and whether the patient would have met practice guideline criteria for outpatient enoxaparin therapy. A total of 266 patients were either admitted to the hospital for DVT or experienced DVT during their hospitalization. Of 266 DVT patients, 73 (27%) received enoxaparin. Sixty-four (88%) patients receiving enoxaparin met practice guideline criteria. Nine patients (12%) who did not meet criteria also received the drug. Major bleeding occurred in 3 patients (4%) receiving enoxaparin; one patient had a life-threatening hemorrhage. Two of the three patients with major bleeding had contraindications to enoxaparin use. Only 45% of our DVT patients were appropriate candidates for outpatient enoxaparin therapy. We conclude that in tertiary-care hospitals with acutely ill patients, most DVT patients will not be candidates for outpatient therapy with enoxaparin. Limitations to enoxaparin use are not widely appreciated.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 2000:833901 CAPLUS
DN 134:116
TI Low molecular weight **heparins**: are they superior to unfractionated **heparins** to prevent and to **treat** deep vein **thrombosis**?
AU Boneu, Bernard
CS Haematology Laboratory, Rangueil Hospital, Toulouse, 31403, Fr.
SO Thrombosis Research (2000), 100(2, Vessels 4), V113-V120
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier Science Inc.
DT Journal; General Review
LA English

AB A review with 41 refs. In many countries, low mol. wt. **heparins** (LMWHs) have replaced unfractionated **heparin** (UH) for prevention and treatment of **venous** thromboembolism. The present paper reviews the possible advantages of LMWHs over UH. In spite of their lower mol. wt. distribution, LMWHs are functionally more heterogeneous than UH. Their anti-Xa/anti-IIa ratio varies significantly, and the injection of the same dose generates different anti-Xa activities and activated partial thromboplastin time (APTT) prolongations. Their pharmacodynamic properties account for their more convenient use in comparison with UH; however, there is a risk of accumulation in case of renal insufficiency. Even if they are less anticoagulant on the basis of the APTT prolongation, they are not less pro-hemorrhagic than UH. LMHWs are probably less immunogenic and probably induce less osteoporosis. Several meta-analyses published between 1992 and 1999 indicate that LMWHs are as efficient as UH in preventing postoperative deep vein **thrombosis** (DVT) in general surgery and more efficient than UH in preventing DVT in orthopedic surgery and treating established DVT.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 2000:630687 CAPLUS
DN 134:125744
TI Frequency of major hemorrhage in patients treated with unfractionated intravenous **heparin** for deep **venous thrombosis** or pulmonary embolism: A study in routine clinical practice
AU Zidane, Majida; Schram, Miranda T.; Planken, Erwin W.; Molendijk, Wim H.; Rosendaal, Frits R.; Van Der Meer, Felix J. M.; Huisman, Menno V.
CS Department of General Internal Medicine, Leiden University Medical Center, Leiden, Neth.
SO Archives of Internal Medicine (2000), 160(15), 2369-2373
CODEN: AIMDAP; ISSN: 0003-9926
PB American Medical Association
DT Journal
LA English
AB The rate of major hemorrhage during the initial treatment with unfractionated **heparin** (UFH) in patients with deep **venous thrombosis** (DVT) and pulmonary embolism (PE) in routine clin. practice is understudied. In recent clin. trials an overall av. of 3.8% was reported. However, the incidence of this complication in routine patient care might be higher owing to less strict patient selection and lack of standardization in the administration of **heparin**. We have detd. major bleeding rates during **heparin** treatment for DVT or PE in routine practice and compared these rates with data from clin. trials. Data on the occurrence of major hemorrhage were retrieved according to strict criteria from the records of patients who had received continuous i.v. UFH therapy to **treat** objectively documented DVT or PE in 3 hospitals. After exclusion of 29 patients because of lack of objective diagnosis of DVT or PE and 25 patients because of initial treatment with low-mol.-wt. **heparin**, 424 consecutive patients were available for detailed anal. Among them, 17 patients (4.0%; 95% confidence interval, 2.1%-5.9%) experienced major hemorrhage during UFH treatment, which in most patients occurred at the end of planned **heparin** therapy; one of the hemorrhages was fatal. Six patients (1.4%; 95% confidence interval, 0.3%-2.5%) developed clin. suspected recurrent **venous** thromboembolism (fatal in 1 case) during UFH treatment or within 7 days' cessation. Administration of continuous i.v. UFH in patients with DVT or PE in routine clin. practice leads to a major bleeding rate of 4.0%. This rate is comparable to the rate of major bleeding in patients who received UFH in clin. trials. Our findings are relevant to the discussion of major bleeding rates in patients with DVT and PE treated in daily clin. practice with s.c. low-mol.-wt. **heparin** and newer antithrombotic drugs.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 2000:111349 CAPLUS
DN 132:117373
TI Outpatient treatment of pulmonary embolism with dalteparin
AU Kovacs, M. J.; Anderson, D.; Morrow, B.; Gray, L.; Touchie, D.; Wells, P. S.
CS London Health Sciences Center, Univ. Western Ontario, London, ON, N6A 4G5, Can.
SO Thrombosis and Haemostasis (2000), 83(2), 209-211
CODEN: THHADQ; ISSN: 0340-6245
PB F. K. Schattauer Verlagsgesellschaft mbH
DT Journal
LA English
AB Pulmonary embolism is a common complication of deep vein **thrombosis**. It was established that low mol. wt. **heparin** may be used to **treat** deep vein **thrombosis** or pulmonary embolism and randomized studies have established that outpatient management of deep vein **thrombosis** with low mol. wt. **heparin** is at least as effective as in-hospital management with unfractionated **heparin**. This was a prospective cohort study of eligible patients with pulmonary embolism managed as outpatients using dalteparin (200 U/kg s/c daily) for a min. of 5 days and warfarin for 3 mo. Outpatients included those managed exclusively out of hospital and those managed initially for 1-3 days as inpatients who then completed therapy out of hospital. Reasons for admission included hemodynamic instability; hypoxia requiring oxygen therapy; admission for another medical reason; severe pain requiring parenteral analgesia or high risk of major bleeding. Patients were followed for three months for clin. apparent recurrent **venous** thromboembolism and bleeding. Between 3 teaching hospitals, a total of 158 patients with pulmonary embolism were identified. 50 Patients were managed as inpatients and 108 as outpatients. Of the outpatients, 27 were managed for an av. of 2.5 days as inpatients and then completed dalteparin therapy as outpatients. The remaining 81 patients were managed exclusively as outpatients with dalteparin. For all outpatients the overall symptomatic recurrence rate of **venous** thromboembolism was 5.6% (6/108) with only 1.9% (2/108) major bleeds. There were a total of 4 deaths with none due to pulmonary embolism or major bleed. This prospective study suggests that outpatient management of pulmonary embolism is feasible and safe for the majority of patients.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1999:741585 CAPLUS
DN 131:346317
TI Do **heparins** do more than just **treat thrombosis** ? The influence of **heparins** on cancer spread
AU Hettiarachchi, Rohan J. K.; Smorenburg, Susanne M.; Ginsberg, Jeffrey; Levine, Mark; Prins, Martin H.; Buller, Harry R.
CS Dep. Clinical Epidemiology Biostatistics, Academic Medical Center, Univ. Amsterdam, Amsterdam, 1100 DD, Neth.
SO Thrombosis and Haemostasis (1999), 82(2), 947-952
CODEN: THHADQ; ISSN: 0340-6245
PB F. K. Schattauer Verlagsgesellschaft mbH
DT Journal
LA English
AB A beneficial effect of low-mol. wt. **heparin** on the survival of cancer patients with **venous** thromboembolism is indicated in this meta-anal.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS

AN 1999:500686 CAPLUS
DN 131:153560
TI Puerperal septic pelvic thrombophlebitis: incidence and response to **heparin** therapy
AU Brown, Charles E.; Stettler, R. William; Twickler, Diane; Cunningham, F. Gary
CS Departments of Obstetrics and Gynecology, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75235, USA
SO American Journal of Obstetrics and Gynecology (1999), 181(1), 143-148
CODEN: AJOGAH; ISSN: 0002-9378
PB Mosby, Inc.
DT Journal
LA English
AB Before the availability of modern imaging studies the diagnosis of septic pelvic thrombophlebitis causing prolonged puerperal fever was difficult to confirm without surgical exploration. With the use of computed tomog. infection-related pelvic phlebitis can now be confirmed, and this study was designed to det. its incidence after delivery. We also designed a randomized clin. trial to evaluate the efficacy of **heparin** added to antimicrobial therapy for treatment of women with septic phlebitis. We studied women who had pelvic infection and fever that persisted after 5 days despite adequate antimicrobial therapy with clindamycin, gentamicin, and ampicillin. After giving consent study participants underwent abdominopelvic computed tomog. imaging. Women with pelvic thrombophlebitis were randomly assigned to 1 of 2 management schemes that included continuation of antimicrobial therapy, either alone or with the addn. of **heparin**, until the temp. was .ltoreq.37.5.degree. for 48 h. During the 3-yr study period 44,922 women were delivered at Parkland Hospital; among these 8535 (19%) were delivered by the cesarean route. There were 69 women who met criteria for prolonged infection, and 15 (22%) of these were found to have septic pelvic thrombophlebitis. Four had infection after vaginal delivery and 11 had been delivered by the cesarean route. Of 14 women randomly assigned to therapy, 8 were assigned to receive continued antimicrobial therapy without the addn. of **heparin** and the other 6 were assigned to receive **heparin** therapy in addn. to the antimicrobial agents. According to an intent-to-**treat** anal. there was no significant difference between the responses of women with pelvic infection who were and were not given **heparin** therapy. Specifically, women not given **heparin** were febrile for 140.+-.39 h compared with 134.+-.65 h for women who received **heparin** (P =.83). Duration of hospitalization was also similar between the 2 groups at 10.6.+-.1.9 days for those with **thrombosis** who were given antimicrobial agents alone and 11.3.+-.1.2 days for women who also received **heparin** (P >.5). The 54 women with persistent fever but without computed tomog. evidence of septic pelvic thrombophlebitis were hospitalized for a mean of 12.0.+-.4.1 days, compared with 10.9.+-.2.9 days for women in whom **thrombosis** was diagnosed (P =.14). These women were followed up for .gtoreq.3 mo post partum and none showed evidence of reinfection, embolic episodes, or postphlebitic syndrome. The overall incidence of septic pelvic thrombophlebitis was 1:3000 deliveries. The incidence was about 1:9000 after vaginal delivery and 1:800 after cesarean section. Women given **heparin** in addn. to antimicrobial therapy for septic thrombophlebitis did not have better outcomes than did those for whom antimicrobial therapy alone was continued. These results also do not support the common empiric practice of **heparin** treatment for women with persistent postpartum infection.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1998:802424 CAPLUS
DN 130:191655
TI Limitations of conventional treatment options for **heparin** -induced thrombocytopenia

AU Warkentin, Theodore E.
CS Department of Pathology, McMaster University, Hamilton, ON, Can.
SO Seminars in Hematology (1998), 35(4, Suppl. 5), 17-25
CODEN: SEHEA3; ISSN: 0037-1963
PB W. B. Saunders Co.
DT Journal
LA English
AB **Thrombosis** is a common and potentially serious complication of immune-mediated **heparin**-induced thrombocytopenia (HIT). Discontinuation of **heparin** is a simple and important maneuver in patients with suspected HIT. Unfortunately, **thrombosis** often occurs even in those patients in whom **heparin** was discontinued because of thrombocytopenia alone ("isolated" HIT). It therefore is reasonable to consider prophylactic anticoagulation with an alternate anticoagulant in patients with suspected HIT, esp. if their initial indication for anticoagulation persists. For patients with **thrombosis** complicating HIT, conventional treatment options often have important limitations. Warfarin has a slow onset of action, and its use in patients with acute HIT and deep **venous thrombosis** has been assocd. with the devastating syndrome of **venous** limb gangrene. Ancrod, a defibrinogenating snake venom with thrombin-like activity, has also been used to **treat** HIT. However, this agent does not inhibit thrombin generation in HIT, which could explain why some patients who have been treated with this agent have developed certain adverse clin. events, such as warfarin-assocd. **venous** limb gangrene. The use of low-mol.-wt. **heparin** (LMWH) to **treat** patients with HIT is limited by their high rate (up to 100%) of in vitro cross-reactivity with HIT sera, and the relatively frequent occurrence of new or recurrent thrombocytopenia or **thrombosis** during treatment of HIT with this class of agents. In contrast, the mixt. of anticoagulant glycosamingoglycans known as danaparoid sodium has a much lower frequency of in vitro cross-reactivity with HIT sera (10% to 40%, depending upon the sensitivity of the assay). Moreover, clin. significant cross-reactivity during treatment with danaparoid appears to be uncommon, even in patients in whom in vitro cross-reactivity is demonstrable.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1998:740853 CAPLUS
DN 130:162922
TI Comparison of two low-molecular-weight **heparins** for the prevention of postoperative **venous** thromboembolism after elective hip surgery
AU Planes, A.; Vochelle, N.; Fagola, M.; Bellaud, M.
CS the Reviparin Study Group, Department of Orthopaedics, Clinique Radio, La Rochelle, 17028, Fr.
SO Blood Coagulation & Fibrinolysis (1998), 9(6), 499-505
CODEN: BLFIE7; ISSN: 0957-5235
PB Lippincott-Raven Publishers
DT Journal
LA English
AB Low-mol.-wt. **heparins** (LMWHs) have been shown to be effective in the prevention of deep vein **thrombosis** (DVT) after major orthopedic surgery, such as total hip replacement (THR). The efficacy and safety of two LMWHs, reviparin and enoxaparin, were compared in a prospective, double-blind, double-dummy study involving 498 patients undergoing total hip replacement. Drugs were given preoperatively in doses of 4200 IU anti-Xa for reviparin and 40 mg (approx. 4000 IU anti-Xa) for enoxaparin. The endpoint for the assessment of efficacy was venog. confirmed DVT. The endpoint for the assessment of safety was clin. important bleeding during study treatment. There were evaluable venograms for 460 patients (93%). Of these 460 patients only 416 fulfilled the study protocol. A total of 39 DVTs (9%) occurred in this per protocol

group of patients, 21 (10%) in the reviparin group, and 18 (9%) in the enoxaparin group. The incidence of proximal DVT was 6% in each group. The two treatments were found to be equiv. in terms of efficacy. For the 460 patients with venograms (intent-to-**treat**) **venous thrombosis** occurred in 49 patients (11%). Of the 230 patients randomly assigned to reviparin, 27 had a DVT (12%), whereas 22 of the 230 enoxaparin patients (10%) had a DVT. The incidence of proximal DVT was 6% in both groups. Again, the two treatment groups were clin. equiv. in efficacy. Major bleeding complications occurred in two enoxaparin- and one reviparin-treated patient. Peri- and postoperative blood loss and blood transfusions were similar in both treatment groups. The reviparin-treated patients had fewer hematomas, bruisings and higher red cell counts and lower Hb levels than the enoxaparin-treated patients.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1997:764724 CAPLUS
DN 128:43657
TI Manipulation of coagulation factors in acute stroke
AU Meschia, James F.; Biller, Jose
CS Department of Neurology, Indiana University Medical Center, Indianapolis, IN, USA
SO Drugs (1997), 54(Suppl. 3, Haematological/Rheological and Neurological Aspects of Ischaemic Stroke), 71-82
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis
DT Journal
LA English
AB In patients with an acute cerebral infarction, anticoagulation may spare tissue in the ischemic penumbra from irreversible necrosis by preventing thrombus extension from a vascular bed with good collateral circulation to one with poor collateral circulation. In addn. to the possibility of limiting infarct vol., anticoagulation may be given acutely to prevent early recurrent cerebral infarction or to prevent or **treat** thrombus outside the nervous system (i.e. deep **venous thrombosis** or pulmonary embolus). In one controlled trial of a low-mol.-wt. **heparin**, administration of nadroparin calcium within 48 h of onset of cerebral infarction decreased the combined incidence of dependency and all-cause mortality at 6 mo. Another controlled trial in patients with cerebral **venous thrombosis** demonstrated the benefit of continuous i.v. adjusted-dose unfractionated (UF) **heparin** compared with placebo. Although results of anticoagulation appear promising in patients with acute cerebral infarction and cerebral **venous thrombosis** , the benefits of these agents remain unconfirmed. The results of large multicenter trials using a heparinoid (ORG 10172) and s.c. UF **heparin** in patients with acute cerebral infarction are expected within the year.

L13 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1997:681470 CAPLUS
TI Surgical alternatives in pulmonary embolism
AU Jakob, H.; Kamler, M.; Vahl, C. -F.; Lange, R.; Tanzeem, A.; Hagl, S.
CS Abteilung fur Herzchirurgie, Ruprecht-Karls-Universitat Heidelberg, Heidelberg, Germany
SO Fibrinolysis Proteolysis (1997), 11(Suppl. 2, Update in Thrombolysis), 197-203
CODEN: FBPRFP
PB Churchill Livingstone
DT Journal
LA English
AB Surgical intervention in pulmonary embolism (PE) is still assocd. with an overall fatal outcome of 30-60% depending on the hemodynamic condition of the patient when operated. Thus conservative treatment using

heparin or fibrinolytic agents has become the treatment of choice. In grade IV PE, however, surgical treatment might be a live-saving option in cases of shock or contraindication to fibrinolysis. The objective of this study was to evaluate the results of a modified surgical approach to **treat** fulminant PE. From May 1993 to June 1996 12 patients with fulminant PE were operated under emergency conditions, with six patients (50%) under or after cardiopulmonary resuscitation (CPR). A modified surgical approach was performed allowing for selective thrombectomy from both pulmonary artery systems down to the segmental artery level as well as simultaneous closed **venous** thrombectomy with clearance of the major body veins during extracorporeal circulation (ECC). In two cases the acute form of PE was assocd. with unilateral, chronic and subtotal obstructing embolization requiring deep hypothermic circulatory arrest and pulmonary thrombendarterectomy. In six patients systolic pulmonary artery pressure (PAP) was measured immediately prior to start of ECC, prior to closure of the chest and after an interval of 3-6 days. It could be demonstrated that an ad hoc fall from 53.3 .+-. 10.8 mmHg to 29.7 .+-. 13.1 mmHg (P = 0.007) resulted, which continued during the first postoperative days to 23.3 .+-. 6.5 mmHg. All but one polytraumatized patient, in whom no pulmonary embolism was found at surgery, survived (92%). One patient died after prolonged preoperative CPR 4 mo after surgery due to permanent neurol. damage, another patient died 20 mo after surgery due to malignancy. All other patients (follow-up range 9-45 mo) are fully rehabilitated and free of PE recurrency under coumadin medication, with three patients having required the placement of a LGM caval filter for ongoing iliac vein **thrombosis**. Fast and accurate diagnosis of grade IV PE still is problematic in an emergency situation. However, this study concluded that the modified surgical approach with complete desobliteration of the pulmonary artery system as well as simultaneous **venous** thrombectomy represents a safe and highly efficient therapeutic option in grade IV PE to immediately relieve acute pulmonary artery hypertension and to prevent early embolic recurrence. Long-term freedom from re-embolization is warranted by the differentiated use of caval filters and continued anticoagulation.

L13 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1997:295214 CAPLUS
DN 126:324723
TI Low molecular weight **heparins**: implications for anesthesia and recovery
AU Llau, J. V.; Hoyas, L.; Ezpeleta, J.; Garcia-Polit, J.; Barbera, M.; Santes, M. J.
CS Servicio Anestesia-Reanimacion, Terapia Dolor, Hospital Clinico Universitario Valencia, Spain
SO Revista Espanola de Anestesiologia y Reanimacion (1997), 44(2), 70-78
CODEN: REANBJ; ISSN: 0034-9356
PB Ediciones Doyma SA
DT Journal; General Review
LA Spanish
AB A review with 142 refs. Low mol. wt. **heparins** are a group of drugs that have only recently been introduced in clin. practice. The are widely used for prophylaxis in thromboembolic disease and are being employed increasingly to **treat** established **venous** **thrombosis**. One way in which these drugs are often used is for prophylaxis in the perioperative period for patients at high risk of developing **venous** thromboembolism, and the anesthesiologist must therefore be familiar with the main aspects of this application. We review pharmacol. characteristics of these drugs as well as the literature on low mol. wt. **heparins**, stressing points of main interest to the anesthesiologist and intensive care recovery unit specialist, namely adverse effects (mainly bleeding) and the implications that use of low mol. wt. **heparin** will have on choice of anesthetic (in particular the dilemma of whether to use local-regional anesthesia).

L13 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2002 ACS

AN 1996:653004 CAPLUS
TI A multicenter randomized double-blind study of enoxaparin compared with unfractionated **heparin** in the prevention of **venous** thromboembolic disease in elderly in-patients bedridden for an acute medical illness
AU Bergmann, Jean Francois; Neuhart, Eric
CS Clinique Therapeutique, Hopital Lariboisiere, Paris, F-75010, Fr.
SO Thromb. Haemostasis (1996), 76(4), 529-534
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
AB A multicenter, randomized double-blind study compared in two parralel groups the efficacy and safety of a low mol. wt. **heparin** (LMWH) enoxaparin 20 mg once daily, with unfractioned **heparin** (UFH) 5000 IU twice daily, administered s.c. for 10 days, in the prevention of **venous thrombosis** disease in 442 hospitalized elderly patients bedridden for an acute medical illness. The main efficacy endpoint was defined as the occurrence of **venous thrombosis**, diagnosed by a daily fibrinogen uptake test, and/or documented clin. pulmonary embolism. Intention-to-**treat** anal. of efficacy showed that the incidence of **venous** thromboembolic events was low: 4.8% (10/207) in the LMWH group (9 episodes of isotopic **venous thrombosis** and one of scintigraphic pulmonary embolism), and 4.6% (10/216) in the UFH group (10 episodes of isotopic **venous thrombosis**). The two treatments were equiv., where equivalence was defined as a max. difference of 7% between the two groups ($p = 0.0005$). There were no significant differences in terms of safety between the 216 patients in the LMWH group and the 223 patients in the UFH group who received at least one injection of the randomized treatment. During the study period, 15 patients (3.4%) died (7 in the LMWH group and 8 in the UFH group): 2 sudden deaths, one in each group, including one case in which pulmonary embolism could not be excluded since no autopsy was performed, and 13 others deaths unrelated to the study treatments. Six patients (1.4%) presented a bleeding complication: 2 (0.9%) in the enoxaparin group (one major and one minor hemorrhage), and 4 (1.8%) in the UFH group (2 major and 2 minor hemorrhages). These results indicate that s.c. enoxaparin 20 mg once daily for 10 days is as effective and well tolerated at s.c. UFH 5000 IU twice daily in the prevention of **venous** thromboembolic disease in bedridden elderly in-patients presenting an acute medical illness.

L13 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1996:447431 CAPLUS
DN 125:131373
TI Prevention and treatment of **venous** thromboembolism
AU Pineo, Graham F.; Hull, Russell D.
CS Calgary General and Foothills Hospitals, University Calgary, Calgary, AB, Can.
SO Drugs (1996), 52(1), 71-92
CODEN: DRUGAY; ISSN: 0012-6667
DT Journal; General Review
LA English
AB A review with 163 refs. All patients at moderate to high risk for the development of **venous** thromboembolism should receive prophylaxis. The approaches of proven value include low-dose **heparin**, low mol. wt. **heparin**, oral anticoagulants and intermittent pneumatic compression. The use of one of the cited **heparin** nomograms will ensure that all patients are rapidly brought within the therapeutic range. Because of the varying sensitivities of thromboplastins, each lab. should establish a therapeutic range using the activated partial thromboplastin time (APTT) which will correspond to 0.2 to 0.4 U/mL of **heparin**. Const. vigilance and a high level of suspicion are necessary to establish the clin. diagnosis of **heparin**-induced thrombocytopenia, and to institute appropriate therapy. Physicians should be aware of the sensitivity of the

thromboplastin being used in the performance of the International Normalized Ratio (INR). Care must be taken to ensure that patients are maintained within the target therapeutic range for INR (in most cases 2 to 3) by frequent detn. of the INR and appropriate adjustments of warfarin dosage. Low mol. wt. **heparin** is the recommended approach to the initial management of **venous** thromboembolism where these agents are available. Patients with an acute episode of **venous** thromboembolism should receive warfarin therapy for at least 3 mo. At the present time it is reasonable to **treat** the first recurrence with oral anticoagulants for a period of 12 mo and indefinitely for more than 1 recurrence. For selected patients with acute massive pulmonary embolism, thrombolytic therapy with one of the available agents is recommended. However, the role of thrombolytic therapy in patients with proximal **venous thrombosis** remains unclear. In selected patients with acute **venous** thromboembolism who have contra-indications to anticoagulant therapy or who have objectively documented recurrent disease while on adequate therapy, the insertion of an inferior vena cava filter is recommended.

L13 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1995:917610 CAPLUS
DN 124:20759
TI Recent developments in antithrombotic agents
AU Fareed, Jawed; Callas, Demetra D; Hoppensteadt, Debra; Jeske, Walter; Walenga, Jeanine M
CS Departments Pathology, Loyola University Chicago, Maywood, IL, 60153, USA
SO Expert Opin. Invest. Drugs (1995), 4(5), 389-412
CODEN: EOIDER; ISSN: 0967-8298
DT Journal; General Review
LA English
AB A review with 103 refs. During the past decade, many significant developments in the clin. management of thrombotic and vascular disorders have occurred. In particular, several newer approaches for the prophylactic and therapeutic management of such disorders as **venous thrombosis**, acute myocardial infarction and stroke have been introduced. This has only been possible due to the understanding of the mol. mechanisms involved in the thrombogenic process which plays a key role in the pathophysiol. of thrombotic and vascular disorders. With the increased knowledge of the pathophysiol. of **thrombosis** have come advances in drug treatment possibilities. Advances in biotechnol. and sepn. techniques have contributed to the development of many newer antithrombotic, anticoagulant and thrombolytic drugs. Many new drugs and devices based on newer concepts are currently being tested in various clin. trials. Hirudin, hirulog, GpIIb/IIIa targeting antibodies and tissue factor pathway inhibitor (TFPI), are some examples. From these current developments, it can be appreciated that antithrombotic drugs represent a wide spectrum of natural, synthetic, semisynthetic and biotechnol. produced agents with marked differences in chem. compn., physicochem. properties, biochem. actions and pharmacol. effects. The use of phys. means to **treat** thrombotic disorders and advanced means of drug delivery add to the expanding nature of treatment. The endogenous actions of the antithrombotic drugs are quite complex. It is no longer valid to assume that an antithrombotic drug must produce an anticoagulant action in blood, as do the classical **heparin** and oral anticoagulants. Many of these new drugs do not produce any alteration of currently measurable blood clotting parameters, yet they are effective therapeutic agents because of their interactions with the elements of the blood and the vasculature. Another perspective is that several of these agents require endogenous transformation to become active products. Therefore, it becomes important to rely on the pharmacodynamic actions of these agents rather than on other in vitro characteristics to assess potency or efficacy. Hematol. and vascular modulation play a key role in the mediation of the antithrombotic actions of these drugs involving red cells, white cells, platelets, endothelial cells and blood proteins. Thus, an optimal antithrombotic drug/approach

will include the targeting of all possible sites involved in thrombogenesis. Polytherapeutic approaches utilizing combinations of drugs may turn out to be the most effective in the management of thrombotic disorders.

L13 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1995:264292 CAPLUS
DN 122:45723
TI Pharmacological properties of CY 216 and of its ACLM and BCLM components in the rabbit
AU Peyrou, V.; Lormeau, J. C.; Caranobe, C.; Gabaig, A. M.; Crepon, B.; Saivin, S.; Houin, G.; Sie, P.; Boneu, B.
CS Laboratoire de Recherche sur l'Hemostase et la Thrombose, Hospital Purpan, Toulouse, F-31059, Fr.
SO Thromb. Haemostasis (1994), 72(2), 268-74
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
AB This study compares some in vivo pharmacol. properties of CY 216 and of its ACLM and BCLM components having a mol. wt. above and below 5.4 kDa resp. The anti-factor Xa/antithrombin ratio of these compds. detd. in a rabbit plasma system were 2.5 and 1.2 for CY 216 and ACLM resp. while BCLM was devoid of anti-thrombin effect. After bolus i.v. injection, continuous infusion, and s.c. administration the clearances of anti-factor Xa activity generated by ACLM were, on the av., 2 and 1.5 times higher than those generated by BCLM and CY 216 resp. The clearances of the anti-thrombin activity were comparable for CY 216 and ACLM, and higher than those of the antifactor Xa activity. The duration of the antithrombotic effect was investigated in the Wessler model after a single s.c. injection of 1000 anti-factor Xa units of one of the compds. Using thromboplastin as thrombogenic stimulus, the most efficient agent was ACLM and the antithrombotic activity was essentially correlated to the circulating anti-thrombin activity. Using human serum as thrombogenic stimulus, ACLM and BCLM were more efficient than CY 216 and the antithrombotic activity was mainly correlated to the anti-factor Xa activity. The ability of the 3 compds. to inhibit **venous thrombosis** growth was compared: they were found equipotent and the antithrombotic effect was independent of the anti-thrombin activity. The prohemorrhagic properties were compared in the rabbi ear model. The activity of the 3 compds. were comparable and significantly less prohemorrhagic than unfractionated **heparin**. These results suggest that the hemorrhagic potential of unfractionated **heparin** and of LMWH is independent of the anti-thrombin and anticoagulant activity, but related to the mol. wt. These observations indicate that factor Xa inhibition is a valuable target to prevent and to **treat venous thrombosis** and that the anti-factor Xa activity of a low mol. wt. **heparin** (LMWH) largely contributes to its antithrombotic effect.

L13 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2002 ACS
AN 1993:160781 CAPLUS
DN 118:160781
TI Effects of **heparin**, dermatan sulfate and of their association on the inhibition of **venous thrombosis** growth in the rabbit
AU Carrie, D.; Caranobe, C.; Gabaig, A. M.; Larroche, M.; Boneu, B.
CS Lab. Hemostase, Cent. Transfus. Sang., Toulouse, 31052, Fr.
SO Thromb. Haemostasis (1992), 68(6), 637-41
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
AB This study compares the ability of unfractionated **heparin**, of dermatan sulfate, and of their simultaneous administration delivered as continuous i.v. infusion or as a single bolus injection to inhibit the growth of a standardized **venous thrombosis** in the

rabbit. When delivered as continuous i.v. infusion for 4 h, **heparin** and dermatan sulfate inhibited thrombus growth in a dose-dependent manner. The max. antithrombotic effect of **heparin** was achieved at the dose of 0.15 mg kg-1 h-1 (25 U kg-1 h-1) which generated a mean plasma concn. of 1.8 .mu.g mL-1 (0.31 U mL-1) and a 1.8-fold prolongation of the activated partial thromboplastin time (APTT) in comparison to the pretreatment value. A comparable antithrombotic effect was obtained with dermatan sulfate at the dose of 2 mg kg-1 h-1. This dose generated a mean plasma concn. of 30 .mu.g mL-1 and a 1.3 fold APTT prolongation. Increasing these doses up to 10-fold did not improve the antithrombotic effect which did not overpass 60-70% of the controls. When the compds. were delivered simultaneously, the max. antithrombotic effect (64%) was obtained with the following assocn.: 0.06 mg kg-1 h-1 (10 U kg-1 h-1) for **heparin** and 1 mg kg-1 h-1 for dermatan sulfate. Increasing these doses up to 4 to 5-fold did not improve the antithrombotic effect. **Heparin**, dermatan sulfate and the assocn. of both were also delivered as single bolus injections and the resultant antithrombotic effect was detd. 4 h after saline infusion. Bolus doses of 0.15 and 0.30 mg kg-1 (25 and 50 U kg-1) of **heparin** or of 1 and 2 mg kg-1 of dermatan sulfate were ineffective. In contrast, the assocn. of dermatan sulfate (2 mg kgl-1) to **heparin** (0.15 or 0.30 mg kg-1) generated antithrombotic effects of 61 and 64% resp. in the absence of detectable residual plasma anticoagulant activities, 1 h after the bolus injection. These studies indicate that (1) under continuous i.v. regimen, dermatan sulfate is as effective as **heparin** to inhibit **venous** thrombus growth when delivered at a 13-fold higher dose on a wt. basis; (2) the coadministration of the two compds. under the same regimen does moderately improve the antithrombotic effect; (3) while each of these compds. were ineffective when delivered as a single bolus, their coadministration generated a dramatic antithrombotic effect for at least 4 h; (4) simultaneous activation of antithrombin III and of **heparin** cofactor II may therefore represent a valuable strategy to **treat** an established deep vein **thrombosis**.

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=> s l1 and weight
         87192 WEIGHT
          7539 WEIGHTS
         92611 WEIGHT
                (WEIGHT OR WEIGHTS)
       1265987 WT
         94137 WTS
       1314638 WT
                (WT OR WTS)
       1340969 WEIGHT
                (WEIGHT OR WT)
L14       6354 L1 AND WEIGHT

=> s l14 and mean
        357744 MEAN
        439559 MEANS
        785373 MEAN
                (MEAN OR MEANS)
L15        379 L14 AND MEAN

=> s l15 and 2000
        144677 2000
L16          2 L15 AND 2000

=> dis l16 1-2 bib abs

L16  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2002 ACS
AN   2001:181817  CAPLUS
DN   134:361172
TI   Anticoagulant Pharmacodynamics of Tinzaparin Following 175 IU/kg
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Subcutaneous Administration to Healthy Volunteers

AU Barrett, J. S.; Hainer, J. W.; Kornhauser, D. M.; Gaskill, J. L.; Hua, T. A.; Sprogel, P.; Johansen, K.; van Lier, J. J.; Knebel, W.; Pieniaszek, H. J.

CS DuPont Pharmaceuticals, Wilmington, Newark, DE, 19714, USA

SO Thrombosis Research (2001), 101(4), 243-254
CODEN: THBRAA; ISSN: 0049-3848

PB Elsevier Science Inc.

DT Journal

LA English

AB Tinzaparin, a sodium salt of a low-mol.-**wt. heparin** (LMWH) produced via heparinase digestion, is used for the treatment of deep vein thrombosis (DVT) and pulmonary embolism in conjunction with warfarin for the prevention of DVT in patients undergoing hip or knee replacement surgery, and as an anticoagulant in hemodialysis circuits. Its av. mol. **wt.** ranges between 5500 and 7500 daltons (Da); the percentage of chains with mol. **wt.** lower than **2000** Da is not more than 10% in the marketed tinzaparin formulation. While this fraction is generally considered pharmacol. inactive, this has never been evaluated in vivo. The importance of the <**2000** Da fraction on the anticoagulant pharmacodynamics of tinzaparin assessed by anti-Xa and anti-IIa activity was studied in a two-way crossover trial. In this trial, 30 healthy volunteers received a single 175 IU/kg s.c. administration of tinzaparin contg. approx. 3.5% of the <**2000** Da fraction and a tinzaparin-like LMWH contg. 18.3% of the <**2000** Da fraction. The anti-Xa/anti-IIa ratios of the drug substances were comparable at 1.5 and 1.7 for tinzaparin and the tinzaparin-like LMWH, resp. Both formulations were safe and well tolerated. **Mean** max. plasma anti-Xa activity (Amax) was approx. 0.818 IU/mL at 4 h following tinzaparin injection. **Mean** max. plasma anti-IIa activity was 0.308 IU/mL at 5 h postdose. Intersubject variation was lower (<18% for both anti-Xa and anti-IIa metrics) than in previous fixed-dose administration studies. There was no correlation between anti-Xa or anti-IIa AUC or Amax and bodyweight in the present study supporting the **wt.**-adjusted dosing regimen. Individual anti-Xa and anti-IIa profiles following the single 175 IU/kg s.c. administration of the tinzaparin-like LMWH were similar to that obtained with tinzaparin. Based on av. equivalence criteria, the two LMWH prepns. were detd. to be bioequivalent using either anti-Xa or anti-IIa activity as biomarkers. The calcd. intrasubject variabilities were low (<14% for anti-Xa activity and <18% for anti-IIa activity) yielding little evidence for a significant Subject.times.Formulation interaction. In summary, anti-Xa and anti-IIa activity following a single s.c. administration of tinzaparin 175 IU/kg to healthy volunteers yielded activity consistent with targeted therapeutic levels derived from previous trials in adult DVT patients. **Wt**.-based dosing for the treatment of DVT appears rational based on the redn. in anti-Xa and anti-IIa variability consistent with the recommendation derived from earlier fixed-dose pharmacokinetic studies. Furthermore, differences in the percentage of mols. in the <**2000** Da mol. **wt.** fraction of tinzaparin do not translate into differences in anti-Xa and anti-IIa activity in vivo.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

AN 1981:581121 CAPLUS

DN 95:181121

TI Low molecular **weight heparins** and their effects in vitro, in experimental models and in humans

AU Fussi, Fernando; Girolami, Antonio; Cella, Giuseppe

CS Hepar Ind., Inc., Franklin, OH, USA

SO Dev. Biochem. (1981), 12(Chem. Biol. Heparin), 535-46
CODEN: DEBIDR; ISSN: 0165-1714

DT Journal

LA English

AB **Heparin** [9005-49-6] extn. and purifn., detn. of **mean** mol. **wts**. of **heparin** from various sources, and mol. **wt**. distribution in different **heparins** were presented, and the biol. activities of the various **heparin** fractions were studied. The anticoagulant and antithrombotic activities of the **heparin** fractions in vitro and in volunteers following s.c. or i.v. administration increased with decreasing mol. **wt**., the most active being a depolymd., reconstituted **heparin** with a mol. **wt**. of 5000-6000. In vivo antithrombotic activity of **heparin** was greater than expected from in vitro expts. The oral, i.p., and i.v. LD50 values for the depolymd., reconstituted **heparin** in mice were >6000, >3000, and >1000 mg/kg, resp.; in rats the resp. values were >6000, >**2000**, and 354 mg/kg.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	112.89	113.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-21.68	-21.68

STN INTERNATIONAL LOGOFF AT 10:42:03 ON 15 JUL 2002

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FILE 'HOME' ENTERED AT 10:44:00 ON 15 JUL 2002

=> file medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 10:44:08 ON 15 JUL 2002

 FILE LAST UPDATED: 13 JUL 2002 (20020713/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s thrombosis
L1        79682 THROMBOSIS

=> s l1 and venous
          99187 VENOUS
L2        18270 L1 AND VENOUS

=> s l2 and treat
          46889 TREAT
           1164 TREATS
          47969 TREAT
                (TREAT OR TREATS)
L3          252 L2 AND TREAT

=> s l3 and heparin
          53740 HEPARIN
           1747 HEPARINS
          53855 HEPARIN
                (HEPARIN OR HEPARINS)
L4           91 L3 AND HEPARIN

=> s l4 and composition
         120753 COMPOSITION
           8698 COMPOSITIONS
         126637 COMPOSITION
                (COMPOSITION OR COMPOSITIONS)
L5            1 L4 AND COMPOSITION

=> dis l5 bib abs

L5   ANSWER 1 OF 1     MEDLINE
AN   96401345     MEDLINE
DN   96401345   PubMed ID: 8807721
TI   Current trends in antithrombotic drug and device development.
AU   Fareed J
CS   Department of Pathology, Loyola University Medical Center, Maywood, IL
     60153, USA.
SO   SEMINARS IN THROMBOSIS AND HEMOSTASIS, (1996) 22 Suppl 1 3-8.  Ref: 26
     Journal code: 0431155. ISSN: 0094-6176.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA   English
```

FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961203

AB During the past decade, many significant developments in the clinical management of thrombotic and vascular disorders have occurred. In particular, several newer approaches for the prophylactic and therapeutic management of such disorders as **venous thrombosis**, acute myocardial infarction, and stroke have been introduced. This has been possible because of the understanding of the molecular mechanisms involved in the thrombogenic process, which plays a key role in the pathophysiology of thrombotic and vascular disorders. With the increased knowledge of the pathophysiology of **thrombosis** have come advances in drug treatment possibilities. Advances in biotechnology and separation techniques have contributed to the development of many newer antithrombotic, anticoagulant, and thrombolytic drugs. Many new drugs and devices based on newer concepts are currently being tested in various clinical trials. Hirudin, hirulog, GPIIb/IIIa targeting antibodies, and tissue factor pathway inhibitor are some examples. From these current developments, it can be appreciated that antithrombotic drugs represent a wide spectrum of natural, synthetic, semisynthetic, and biotechnology-produced agents with marked differences in chemical **composition**, physicochemical properties, biochemical actions, and pharmacologic effects. The use of physical means to **treat** thrombotic disorders and advanced means of drug delivery add to the expanding nature of treatment. The endogenous actions of the antithrombotic drugs are quite complex. It is no longer valid to assume that an antithrombotic drug must produce an anticoagulant action in blood, as do the classical **heparin** and oral anticoagulants. Many of these new drugs do not produce any alteration of currently measurable blood-clotting parameters, yet they are effective therapeutic agents because of their interactions with the elements of the blood and the vasculature. Another perspective is that several of these agents require endogenous transformation to become active products. Therefore, it becomes important to rely on the pharmacodynamic actions of these agents rather than on other in vitro characteristics to assess potency or efficacy. Hematologic and vascular modulation play a key role in the mediation of the antithrombotic actions of these drugs, involving red cells, white cells, platelets, endothelial cells, and blood proteins. Thus, an optimal antithrombotic drug approach will include the targeting of all possible sites involved in thrombogenesis. Antithrombotic and anticoagulant drugs will also be useful in the development of such biomedical devices as stents and other vascular support material. Polytherapeutic approaches utilizing combinations of drugs may turn out to be the most effective in the management of thrombotic disorders.

```
=> s heparin
         53740 HEPARIN
          1747 HEPARINS
L6        53855 HEPARIN
                (HEPARIN OR HEPARINS)

=> s l6 and depolymerization
          2372 DEPOLYMERIZATION
             3 DEPOLYMERIZATIONS
          2375 DEPOLYMERIZATION
                (DEPOLYMERIZATION OR DEPOLYMERIZATIONS)
L7         127 L6 AND DEPOLYMERIZATION

=> s l7 and base
        362334 BASE
         32354 BASES
```

```
        382525 BASE
                  (BASE OR BASES)
L8            2 L7 AND BASE

=> sl7 and phosphazene
SL7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=>  s l7 and phosphazene
             55 PHOSPHAZENE
             12 PHOSPHAZENES
             58 PHOSPHAZENE
                  (PHOSPHAZENE OR PHOSPHAZENES)
L9            0 L7 AND PHOSPHAZENE

=> s l7 and imidazolate
             76 IMIDAZOLATE
              1 IMIDAZOLATES
             77 IMIDAZOLATE
                  (IMIDAZOLATE OR IMIDAZOLATES)
L10           0 L7 AND IMIDAZOLATE

=> s l7 and guanine
          26674 GUANINE
            650 GUANINES
          26933 GUANINE
                  (GUANINE OR GUANINES)
L11           0 L7 AND GUANINE

=> s l7 and guanidine
           7428 GUANIDINE
          13957 GUANIDINES
          18326 GUANIDINE
                  (GUANIDINE OR GUANIDINES)
L12           0 L7 AND GUANIDINE

=> s l7 and phosphorine
              2 PHOSPHORINE
              1 PHOSPHORINES
              3 PHOSPHORINE
                  (PHOSPHORINE OR PHOSPHORINES)
L13           0 L7 AND PHOSPHORINE

=> dis l8 1-2 bib abs

L8   ANSWER 1 OF 2     MEDLINE
AN   2000015905     MEDLINE
DN   20015905   PubMed ID: 10549712
TI   Structural characterization of low molecular weight heparins.
AU   Casu B; Torri G
CS   G. Ronzoni Institute for Chemical and Biochemical Research, Milan, Italy.
SO   SEMINARS IN THROMBOSIS AND HEMOSTASIS, (1999) 25 Suppl 3 17-25.  Ref: 34
     Journal code: 0431155. ISSN: 0094-6176.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA   English
FS   Priority Journals
EM   199912
ED   Entered STN: 20000113
     Last Updated on STN: 20000113
```

Entered Medline: 19991208

AB Low molecular weight **heparins** (LMWHs) obtained by different **depolymerization** processes can be distinguished from each other by characteristic end-residues, which are easily identified and quantified by nuclear-magnetic-resonance (NMR) spectroscopy. NMR spectroscopy characterizes major sulfation patterns as well as minor sequences such as the antithrombin-binding sequence and the linkage region of LMWHs. Artifacts associated with **base**-induced modifications such as the formation of iduronic acid epoxide and aziridine derivatives of N-sulfoglucosamine residues can also be detected. The influence of these modifications on the binding of **heparins** and LMWHs to proteins other than antithrombin are discussed.

L8 ANSWER 2 OF 2 MEDLINE
AN 1999369648 MEDLINE
DN 99369648 PubMed ID: 10440667
TI Immobilization of recombinant heparinase I fused to cellulose-binding domain.
AU Shpigel E; Goldlust A; Efroni G; Avraham A; Eshel A; Dekel M; Shoseyov O
CS The Kennedy Leigh Centre for Horticultural Research and The Otto Warburg Center for Agricultural Biotechnology, The Faculty of Agriculture, The Hebrew University of Jerusalem, P.O. Box 12, Rehovot 76100, Israel.
SO BIOTECHNOLOGY AND BIOENGINEERING, (1999 Oct 5) 65 (1) 17-23.
Journal code: 7502021. ISSN: 0006-3592.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991018

AB Immobilization of biologically active proteins is of great importance to research and industry. Cellulose is an attractive matrix and cellulose-binding domain (CBD) an excellent affinity tag protein for the purification and immobilization of many of these proteins. We constructed two vectors to enable the cloning and expression of proteins fused to the N- or C-terminus of CBD. Their usefulness was demonstrated by fusing the **heparin**-degrading protein heparinase I to CBD (CBD-HepI and HepI-CBD). The fusion proteins were over-expressed in Escherichia coli under the control of a T7 promoter and found to accumulate in inclusion bodies. The inclusion bodies were recovered by centrifugation, the proteins were refolded and recovered on a cellulose column. The bifunctional fusion protein retained its abilities to bind to cellulose and degrade **heparin**. C-terminal fusion of heparinase I to CBD was somewhat superior to N-terminal fusion: Although specific activities in solution were comparable, the latter exhibited impaired binding capacity to cellulose. CBD-HepI-cellulose bioreactor was operated continuously and degraded **heparin** for over 40 h without any significant loss of activity. By varying the flow rate, the mean molecular weight of the **heparin** oligosaccharide produced could be controlled. The molecular weight distribution profiles, obtained from **heparin depolymerization** by free heparinase I, free CBD-HepI, and cellulose-immobilized CBD-HepI, were compared. The profiles obtained by free heparinase I and CBD-HepI were indistinguishable, however, immobilized CBD-HepI produced much lower molecular weight fragments at the same percentage of **depolymerization**. Thus, CBD can be used for the efficient production of bioreactors, combining purification and immobilization into essentially a single step.

=> s l7 and salt
47752 SALT

```
          36115 SALTS
          78709 SALT
                (SALT OR SALTS)
L14           7 L7 AND SALT

=> dis l14 1-7 bib abs

L14  ANSWER 1 OF 7     MEDLINE
AN   96362166     MEDLINE
DN   96362166   PubMed ID: 8720143
TI   Importance of 6-O-sulfate groups of glucosamine residues in
     heparin for activation of FGF-1 and FGF-2.
AU   Ishihara M; Takano R; Kanda T; Hayashi K; Hara S; Kikuchi H; Yoshida K
CS   Seikagaku Corporation, Tokyo Research Institute.
SO   JOURNAL OF BIOCHEMISTRY, (1995 Dec) 118 (6) 1255-60.
     Journal code: 0376600. ISSN: 0021-924X.
CY   Japan
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199610
ED   Entered STN: 19961022
     Last Updated on STN: 19970203
     Entered Medline: 19961010
AB   Treatment of the pyridinium salts of heparin with
     N-methyltrimethylsilyl-trifluoroacetamide (MTSTFA) in pyridine for 2 h at
     various temperatures caused specific 6-O-desulfations from trisulfated
     disaccharide units to various degrees without detectable
     depolymerization or other chemical changes. In order to assess the
     importance of 6-O-sulfate groups in N-sulfated glucosamine (GlcNS)
     residues to promote FGF-1 and FGF-2 activities, various 6-O-desulfated
     (6-O-DS-) heparins were quantitatively examined for activity as
     enhancers or inhibitors of specific FGF-1- and FGF-2-induced proliferation
     of BALB/c3T3 clone A31 (A31) cells and the chlorate-treated cells. The
     present results suggested that a high content of 6-O-sulfate groups in
     GlcNS residues was required for activation of FGF-1, but not FGF-2.
     However, complete 6-O-desulfation of trisulfated disaccharide units in
     heparin resulted in loss of the ability to activate FGF-2,
     although the desulfated product bound strongly to FGF-2.

L14  ANSWER 2 OF 7     MEDLINE
AN   96350442     MEDLINE
DN   96350442   PubMed ID: 8765134
TI   Inhibition of human leukocyte elastase activity by heparins:
     influence of charge density.
AU   Volpi N
CS   Department of Biologia Animale, University of Modena, Italy.
SO   BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Aug 13) 1290 (3) 299-307.
     Journal code: 0217513. ISSN: 0006-3002.
CY   Netherlands
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199609
ED   Entered STN: 19961008
     Last Updated on STN: 20000303
     Entered Medline: 19960924
AB   Heparins with different structures and physico-chemical
     properties were evaluated for their capacity to inhibit human leukocyte
     elastase activity in vitro by using a chromogenic substrate.
     Heparin from bovine intestinal mucosa and heparan sulfate from
     bovine spleen were extracted and purified, and their purity, structures,
     and physico-chemical properties were evaluated. Slow moving and fast
     moving heparin species were obtained by selective precipitation
```

as barium **salt**, and partially desulfated and re-N-sulfated **heparin** was produced by chemical modifications. **Heparins** with different molecular mass (from 950 to 7820), narrow polydispersity and the same charge density were produced by a chemical **depolymerization** process in the presence of free radicals, and further gel-permeation chromatography. **Heparins** strongly inhibit elastase activity, and there is a significant linear dependence between charge density (sulfate-to-carboxyl ratio) and enzymatic activity. We also found a significant linear correlation between the percentage of N-sulfate groups and increased inhibition of elastase activity and between the percentage of iduronic acid and enzymatic activity. **Heparin** samples with a M(r) greater than about 2000-3000 inhibit the HLE activity to the same extent (about 59%) whilst two fractions with a M(r) of 1530 (29% inhibition of HLE activity) and 950 (4% inhibition of HLE activity) have less capacity to produce a decrease in the enzymatic activity.

L14 ANSWER 3 OF 7 MEDLINE
AN 94066102 MEDLINE
DN 94066102 PubMed ID: 8246223
TI Preparation and anti-HIV activity of O-acylated **heparin** and dermatan sulfate derivatives with low anticoagulant effect.
AU Barzu T; Level M; Petitou M; Lormeau J C; Choay J; Schols D; Baba M; Pauwels R; Witvrouw M; De Clercq E
CS Sanofi Recherche-Centre Choay, Gentilly, France.
SO JOURNAL OF MEDICINAL CHEMISTRY, (1993 Nov 12) 36 (23) 3546-55. Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199401
ED Entered STN: 19940201
Last Updated on STN: 19970203
Entered Medline: 19940106
AB In order to increase the ratio of anti-HIV activity to anticoagulant activity, glycosaminoglycan derivatives selectively substituted at OH and/or COOH groups were prepared. Standard **heparin**, **heparin** fragments, or dermatan sulfate were converted to their tributylammonium or tetrabutylammonium **salts**. Their selective O-acylation to various (controlled) degrees was carried out in a homogeneous way in N,N-dimethylformamide using carboxylic acid anhydrides and 4-(dimethylamino)pyridine as catalyst. Esterification of the COOH groups was performed by the addition of alkyl halide to an N,N-dimethylformamide solution of glycosaminoglycan tetrabutylammonium **salts**. The in vitro anticoagulant activity, the activity against HIV-1 and HIV-2 cytopathicity, the cytotoxicity, and the activity on the induction of giant cell formation were determined. O-acylation (O-butyrylation or O-hexanoylation) of the **heparin** fragments obtained by periodate **depolymerization** (compounds 2d and 2e), and their esters (compounds 7i and 7j), yielded products with very low anticoagulant effects in vitro, yet potent activity against both HIV-1 and HIV-2 induced cytopathicity, and low, if any, cytotoxicity. As compared to other anionic polysaccharides, these acylated derivatives are more active as inhibitors of HIV-induced giant-cell formation. Their anti-HIV activity is related to the degree of O-acylation and is mainly due to the inhibition of virus adsorption to the target cells.

L14 ANSWER 4 OF 7 MEDLINE
AN 93186765 MEDLINE
DN 93186765 PubMed ID: 8444841
TI Preparation of affinity-fractionated, **heparin**-derived oligosaccharides and their effects on selected biological activities mediated by basic fibroblast growth factor.
AU Ishihara M; Tyrrell D J; Stauber G B; Brown S; Cousens L S; Stack R J

CS Glycomed Incorporated, Alameda, California 94501.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Mar 5) 268 (7) 4675-83.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199304
ED Entered STN: 19930416
Last Updated on STN: 19930416
Entered Medline: 19930406
AB Homogeneously sized, **heparin**-derived oligosaccharides were prepared from **heparin** following partial **depolymerization** with nitrous acid, reduction with sodium borohydride, and fractionation by gel permeation chromatography. The resulting pools of di-, tetra-, hexa-, octa-, and decasaccharides were sequentially applied to an affinity column of human recombinant basic fibroblast growth factor (bFGF) covalently attached to Sepharose 4B and further fractionated into subpools based on their elution from this column in response to gradients of sodium chloride. In general, pools of smaller **heparin**-derived oligosaccharides required relatively lower **salt** concentration for complete elution, and pools of larger oligosaccharides required higher **salt** concentration. The homogeneously sized pools and affinity-fractionated subpools of **heparin**-derived oligosaccharides were quantitatively assessed as inhibitors or enhancers of specific bFGF-mediated biological activities in five separate assay systems as follows: assay 1, to compete with human lymphoblastoid cells expressing syndecan (RO-12 UC cells) for binding to bFGF-coated wells (Ishihara, M., Tyrrell, D.J., Kiefer, M.C., Barr, P.J., and Swiedler, S.J. (1992) Anal. Biochem. 202, 310-315); assay 2, to inhibit 125I-bFGF binding to "low affinity sites" of adrenocortical endothelial (ACE) cells; assay 3, to inhibit bFGF-induced proliferation of ACE cells; assay 4, to support mitogenic activity of bFGF in a growth stimulation assay of chlorate-treated ACE cells; and assay 5, to enhance the in vitro interaction between 125I-bFGF and the recombinant extra-cellular domain of FGF high affinity receptor. The data derived from the five assay systems demonstrated that **heparin**-derived hexa- and octasaccharides inhibited the interaction between cell surface heparan sulfate proteoglycan and bFGF (assays 1 and 2) and bFGF-induced proliferation of ACE cells (assay 3) but were unable to enhance the binding of bFGF to its high affinity receptor in vitro (assay 5) or to support bFGF-induced mitogenesis in ACE cells (assay 4). These two activities required at least a decasaccharide with high affinity for bFGF.

L14 ANSWER 5 OF 7 MEDLINE
AN 87025697 MEDLINE
DN 87025697 PubMed ID: 3767952
TI A novel mass spectrometric procedure to rapidly determine the partial structure of **heparin** fragments.
AU McNeal C J; Macfarlane R D; Jardine I
NC GM26096 (NIGMS)
GM32938 (NIGMS)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1986 Aug 29) 139 (1) 18-24.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198610
ED Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19861030
AB The molecular weight and degree of sulfation has been obtained for di-,

tetra- and hexasaccharide fragments of **heparin** obtained by enzymatic **depolymerization** of porcine mucosal **heparin**. The sodium **salt** form of the sulfated oligosaccharide is adsorbed onto an immobilized cationic surfactant film which is inserted directly into the mass spectrometer. Analyses are routinely obtained on 25-50 microgram samples in less than an hour. This approach provides rapid confirmatory structural information that is complementary to existing methodologies.

L14 ANSWER 6 OF 7 MEDLINE
AN 78022408 MEDLINE
DN 78022408 PubMed ID: 144018
TI Solvolytic desulfation of glycosaminoglycuronan sulfates with dimethyl sulfoxide containing water or methanol.
AU Nagasawa K; Inoue Y; Kamata T
SO CARBOHYDRATE RESEARCH, (1977 Sep) 58 (1) 47-55.
Journal code: 0043535. ISSN: 0008-6215.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197712
ED Entered STN: 19900314
Last Updated on STN: 19980206
Entered Medline: 19771229
AB A solvolytic desulfation of glycosaminoglycuronan sulfates was developed by treatment of their pyridinium **salts** with dimethyl sulfoxide containing 10% of water or methanol at 80-100 degrees. Chemical and physical studies showed that the solvolytic desulfation is a useful method applicable to all the known glycosaminoglycuronan sulfates without producing **depolymerization** or unfavorable chemical changes in the polysaccharide molecules. An almost completely desulfated, N-acetylated **heparin** (S: 0.12%) was obtained by treatment of an N-desulfated and N-acetylated **heparin** with dimethyl sulfoxide containing 10% of methanol for 2 h at 100 degrees.

L14 ANSWER 7 OF 7 MEDLINE
AN 76116168 MEDLINE
DN 76116168 PubMed ID: 1248016
TI Selective N-desulfation of **heparin** with dimethyl sulfoxide containing water or methanol.
AU Inoue Y; Nagasawa K
SO CARBOHYDRATE RESEARCH, (1976 Jan) 46 (1) 87-95.
Journal code: 0043535. ISSN: 0008-6215.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197604
ED Entered STN: 19900313
Last Updated on STN: 19980206
Entered Medline: 19760430
AB A solvolytic N-desulfation of **heparin** was developed by treatment of its pyridinium **salt** with dimethyl sulfoxide containing 5% of water or methanol for 1.5 h at 50 degrees. Chemical and chromatographic studies showed that the solvolytic desulfation is a useful method for N-desulfation of **heparin** without **depolymerization** of the **heparin** molecule. The partially N-desulfated **heparins** were also obtained by treatment with dimethyl sulfoxide containing 5% of water at 20 degrees, and their anticoagulant activity is related to the degree of N-desulfation.

=> dis hist

```
      (FILE 'HOME' ENTERED AT 10:44:00 ON 15 JUL 2002)

      FILE 'MEDLINE' ENTERED AT 10:44:08 ON 15 JUL 2002
L1         79682 S THROMBOSIS
L2         18270 S L1 AND VENOUS
L3           252 S L2 AND TREAT
L4            91 S L3 AND HEPARIN
L5             1 S L4 AND COMPOSITION
L6         53855 S HEPARIN
L7           127 S L6 AND DEPOLYMERIZATION
L8             2 S L7 AND BASE
L9             0 S L7 AND PHOSPHAZENE
L10            0 S L7 AND IMIDAZOLATE
L11            0 S L7 AND GUANINE
L12            0 S L7 AND GUANIDINE
L13            0 S L7 AND PHOSPHORINE
L14            7 S L7 AND SALT

=> s l7 and purification
         482735 PURIFICATION
            312 PURIFICATIONS
         482833 PURIFICATION
                (PURIFICATION OR PURIFICATIONS)
L15         33 L7 AND PURIFICATION

=> s l15 and peroxide
          28587 PEROXIDE
          13761 PEROXIDES
          38647 PEROXIDE
                (PEROXIDE OR PEROXIDES)
L16           0 L15 AND PEROXIDE

=> s l4 and anti-Xa
         368580 ANTI
              6 ANTIS
         368584 ANTI
                (ANTI OR ANTIS)
           4468 XA
            128 XAS
           4594 XA
                (XA OR XAS)
            708 ANTI-XA
                (ANTI(W)XA)
L17           4 L4 AND ANTI-XA

=> s l4 and anti-IIa
         368580 ANTI
              6 ANTIS
         368584 ANTI
                (ANTI OR ANTIS)
           7418 IIA
              7 IIAS
           7419 IIA
                (IIA OR IIAS)
            156 ANTI-IIA
                (ANTI(W)IIA)
L18           1 L4 AND ANTI-IIA

=> dis l17 1-4 bib abs

L17  ANSWER 1 OF 4     MEDLINE
AN   2001076618     MEDLINE
DN   20508124   PubMed ID: 11053624
```

TI Low molecular weight **heparins**: are they superior to unfractionated **heparins** to prevent and to **treat** deep vein **thrombosis**?.
AU Boneu B
CS Haematology Laboratory, Rangueil Hospital, Toulouse, France.. boneu.b@chu-toulouse.fr
SO THROMBOSIS RESEARCH, (2000 Oct 15) 100 (2) V113-20. Ref: 41
Journal code: 0326377. ISSN: 0049-3848.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111
AB In many countries, low molecular weight **heparins** (LMWHs) have replaced unfractionated **heparin** (UH) for prevention and treatment of **venous** thromboembolism. The present paper reviews the possible advantages of LMWHs over UH. In spite of their lower molecular weight distribution, LMWHs are functionally more heterogeneous than UH. Their **anti-Xa**/anti-IIa ratio varies significantly, and the injection of the same dose generates different **anti-Xa** activities and activated partial thromboplastin time (APTT) prolongations. Their pharmacodynamic properties account for their more convenient use in comparison with UH; however, there is a risk of accumulation in case of renal insufficiency. Even if they are less anticoagulant on the basis of the APTT prolongation, they are not less prohemorrhagic than UH. LMWHs are probably less immunogenic and probably induce less osteoporosis. Several meta-analyses published between 1992 and 1999 indicate that LMWHs are as efficient as UH in preventing postoperative deep vein **thrombosis** (DVT) in general surgery and more efficient than UH in preventing DVT in orthopedic surgery and treating established DVT.

L17 ANSWER 2 OF 4 MEDLINE
AN 1999034309 MEDLINE
DN 99034309 PubMed ID: 9819000
TI Comparison of two low-molecular-weight **heparins** for the prevention of postoperative **venous** thromboembolism after elective hip surgery. Reviparin Study Group.
AU Planes A; Vochelle N; Fagola M; Bellaud M
CS Department of Orthopaedics, Clinique Radio-Chirurgicale du Mail, La Rochelle, France.
SO BLOOD COAGULATION AND FIBRINOLYSIS, (1998 Sep) 9 (6) 499-505.
Journal code: 9102551. ISSN: 0957-5235.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990226
AB Low-molecular-weight **heparins** (LMWHs) have been shown to be effective in the prevention of deep vein **thrombosis** (DVT) after major orthopaedic surgery, such as total hip replacement (THR). The efficacy and safety of two LMWHs, reviparin and enoxaparin, were compared in a prospective, double-blind, double-dummy study involving 498 patients undergoing total hip replacement. Drugs were given preoperatively in doses

of 4200 IU **anti-Xa** for reviparin and 40mg (approximately 4000 IU **anti-Xa**) for enoxaparin. The endpoint for the assessment of efficacy was venographically confirmed DVT. The endpoint for the assessment of safety was clinically important bleeding during study treatment. There were evaluable venograms for 460 patients (93%). Of these 460 patients only 416 fulfilled the study protocol. A total of 39 DVTs (9%) occurred in this per protocol group of patients, 21 (10%) in the reviparin group, and 18 (9%) in the enoxaparin group. The incidence of proximal DVT was 6% in each group. The two treatments were found to be equivalent in terms of efficacy. For the 460 patients with venograms (intent-to-**treat**) **venous thrombosis** occurred in 49 patients (11%). Of the 230 patients randomly assigned to reviparin, 27 had a DVT (12%), whereas 22 of the 230 enoxaparin patients (10%) had a DVT. The incidence of proximal DVT was 6% in both groups. Again, the two treatment groups were clinically equivalent in efficacy. Major bleeding complications occurred in two enoxaparin- and one reviparin-treated patient. Peri- and postoperative blood loss and blood transfusions were similar in both treatment groups. The reviparin-treated patients had fewer haematomas, bruisings and higher red cell counts and lower haemoglobin levels than the enoxaparin-treated patients.

L17 ANSWER 3 OF 4 MEDLINE
AN 96258079 MEDLINE
DN 96258079 PubMed ID: 8688309
TI Low-molecular-weight **heparin** vs. unfractionated **heparin** in femorodistal reconstructive surgery: a multicenter open randomized study. Enoxart Study Group.
AU Samama C M; Gigou F; Ill P
CS Departement d'Anesthesie-Reanimation, Groupe Hospitalier, Pitie-Salpetriere, Paris, France.
SO ANNALS OF VASCULAR SURGERY, (1995) 9 Suppl S45-53. Journal code: 8703941. ISSN: 0890-5096.
CY United States
DT (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY) (RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199608
ED Entered STN: 19960911 Last Updated on STN: 19960911 Entered Medline: 19960829
AB Several clinical trials have been conducted to study the role of low-molecular-weight **heparin** (LMWH) in the prevention and treatment of **venous thrombosis**. In contrast, there have been few studies investigating LMWH in the prophylaxis in arterial **thrombosis**. After informed consent and institutional approval were obtained, 201 consecutive patients scheduled for femorodistal reconstructive surgery under general anesthesia were enrolled in an open randomized multicenter (n = 14) study (from November 1990 to November 1992). Immediately before arterial cross-clamping, patients were given an intravenous bolus of either enoxaparin (ENX), 75 **anti-Xa** IU/kg (n = 100), or unfractionated **heparin** (UFH), 50 IU kg (n = 101). Meanwhile the saphenous vein or a prosthetic graft was flushed with ENX (25,000 **anti-Xa** IU) or UFH (25,000 IU) in 250 ml of saline solution. Subsequent treatment consisted of subcutaneous administration of ENX, 75 **anti-Xa** IU/kg, or UFH, 150 IU kg, beginning 8 hours after the intravenous injection and then every 12 hours thereafter for 10 days. The primary end point was graft patency on day 10 +/- 2 after surgery as assessed clinically and/or by arteriography on day 10 +/- 2 and/or during reintervention or autopsy. Analysis of patients on an intention-to-**treat** basis (patients who received

at least on injection of ENX or UFH and who had at least one end-point evaluation) showed that graft **thrombosis** occurred in 30 of 199 cases: eight (8%) in the ENX group and 22 (22%) in the UFH group (p = 0.009). Among the 131 patients who were evaluated by arteriography before day 12, twelve (9.1%) had graft **thrombosis**: four (6%) in the ENX group and eight (12.5%) in the UFH group (NS). There were no significant differences between the two groups in terms of safety--that is, there were 12 major hemorrhages in each group, and during the follow-up period five patients in the ENX group died compared to nine in the UFH group (NS). These results indicate that ENX is as safe as but more effective than UFH when used for the prevention of early graft **thrombosis** in patients undergoing femorodistal reconstructive surgery.

L17 ANSWER 4 OF 4 MEDLINE
AN 88264894 MEDLINE
DN 88264894 PubMed ID: 2838923
TI A randomized double-blind study between a low molecular weight **heparin** Kabi 2165 and standard **heparin** in the prevention of deep vein **thrombosis** in general surgery. A French multicenter trial.
AU Caen J P
CS Unite 150 INSERM, Hopital Lariboisiere, Paris, France.
SO THROMBOSIS AND HAEMOSTASIS, (1988 Apr 8) 59 (2) 216-20.
Journal code: 7608063. ISSN: 0340-6245.
CY GERMANY, WEST: Germany, Federal Republic of
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 198807
ED Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880729
AB The safety and efficacy of a low molecular weight **heparin** fragment Kabi 2165, given in the dose 2,500 **anti-Xa** units once daily, in preventing postoperative **venous** thromboembolism, was assessed against calcium **heparin** in the dose 5,000 IU twice daily, in a multicenter double blind randomized study. On an intention to **treat** basis 385 patients scheduled for major surgery were included in this study. Six patients (3.1%) out of 195 developed isotopic DVT in the Kabi 2165 group. Corresponding figures for calcium **heparin** was 7 patients (3.7%). There was no statistically significant difference between the two groups with respect to the bleeding variables; blood loss during operation, postoperative drainage, blood transfusion, haemoglobin and haematocrit levels; wound haematoma and haematoma at the injection sites. No patient had to undergo evacuation of wound haematoma or reoperation due to bleeding. It is concluded that one single daily injection of Kabi 2165 provides a convenient safe and effective prophylaxis against thromboembolism in general surgery.

=> dis l18 bib abs

L18 ANSWER 1 OF 1 MEDLINE
AN 2001076618 MEDLINE
DN 20508124 PubMed ID: 11053624
TI Low molecular weight **heparins**: are they superior to unfractionated **heparins** to prevent and to **treat** deep vein **thrombosis**?.
AU Boneu B
CS Haematology Laboratory, Rangueil Hospital, Toulouse, France..
boneu.b@chu-toulouse.fr

SO THROMBOSIS RESEARCH, (2000 Oct 15) 100 (2) V113-20. Ref: 41
Journal code: 0326377. ISSN: 0049-3848.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111
AB In many countries, low molecular weight **heparins** (LMWHs) have replaced unfractionated **heparin** (UH) for prevention and treatment of **venous** thromboembolism. The present paper reviews the possible advantages of LMWHs over UH. In spite of their lower molecular weight distribution, LMWHs are functionally more heterogeneous than UH. Their anti-Xa/**anti-IIa** ratio varies significantly, and the injection of the same dose generates different anti-Xa activities and activated partial thromboplastin time (APTT) prolongations. Their pharmacodynamic properties account for their more convenient use in comparison with UH; however, there is a risk of accumulation in case of renal insufficiency. Even if they are less anticoagulant on the basis of the APTT prolongation, they are not less prohemorrhagic than UH. LMWHs are probably less immunogenic and probably induce less osteoporosis. Several meta-analyses published between 1992 and 1999 indicate that LMWHs are as efficient as UH in preventing postoperative deep vein **thrombosis** (DVT) in general surgery and more efficient than UH in preventing DVT in orthopedic surgery and treating established DVT.

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FULL ESTIMATED COST | 0.21 | 0.21

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STRUCTURE FILE UPDATES: 14 JUL 2002 HIGHEST RN 438526-30-8
DICTIONARY FILE UPDATES: 14 JUL 2002 HIGHEST RN 438526-30-8

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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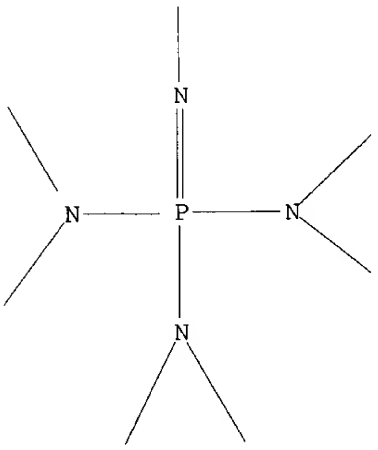

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                        BATCH   **COMPLETE**
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L2            0 SEA EXA SAM L1
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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **5587-42-8** REGISTRY
CN 1H-Imidazole, sodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidazole, sodium deriv
CN Imidazole, sodium salt (8CI)
CN Sodium, imidazol-1-yl- (7CI)
OTHER NAMES:
CN 1-Sodioimidazole
CN Sodium imidazolate
CN Sodium imidazole
CN Sodium imidazolide
DR 88997-03-9, 41253-14-9
MF C3 H4 N2 . Na
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (288-32-4)

Ring System Data

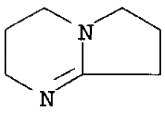
Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3N2	NCNC2	5	C3N2	16.195.24	1

L17 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:524462 CAPLUS
DOCUMENT NUMBER: 127:220360
TITLE: Homoconjugated hydrogen bonds with amidine and guanidine bases. Osmometric, potentiometric and FTIR studies
AUTHOR(S): Galezowski, Wlodzimierz; Jarczewski, Arnold; Stanczyk, Malgorzata; Brzezinski, Bogumil; Bartl, Franz; Zundel, Georg
CORPORATE SOURCE: Faculty of Chemistry, Adam Mickiewicz University, Poznan, PL-60780, Pol.
SOURCE: Journal of the Chemical Society, Faraday Transactions (1997), 93(15), 2515-2518
CODEN: JCFTEV; ISSN: 0956-5000
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five very strong N bases, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), **pKa** = 23.4; 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), **pKa** = 23.9; tetramethylguanidine (TMG), **pKa** = 23.3; 2-phenyl-tetramethylguanidine (PhTMG), **pKa** = 20.6; and 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD), **pKa** = 24.97; have been studied by osmometric measurements which showed that they are monomeric in acetonitrile solns. The consts. of the formation of homoconjugated complexes were detd. by potentiometric measurements. In the IR spectra of the semi-protonated complexes of DBN, DBU and TMG, the homoconjugated N+-H.cntdot..cntdot..cntdot.N .dblharw. N.cntdot..cntdot..cntdot.H-N+ hydrogen bonds cause broad band complexes in the region 3200-2500 cm-1 instead of the expected continua. This spectral peculiarity is discussed.

IT **3001-72-7**, 1,5-Diazabicyclo[4.3.0]non-5-ene
RL: PRP (Properties)
(osmometric, potentiometric and FTIR studies of homoconjugated hydrogen bonds with amidine and guanidine bases.)

RN 3001-72-7 CAPLUS
CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:109180 CAPLUS
DOCUMENT NUMBER: 120:109180
TITLE: Epoxy resin molding materials for sealants
INVENTOR(S): Ichikawa, Masaya; Myatani, Yoshihiro
PATENT ASSIGNEE(S): Matsushita Electric Works Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05239319	A2	19930917	JP 1992-45207	19920303

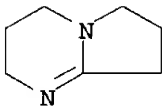
AB The title materials, useful for sealing elec. and electronic parts,

contain basic compds. having pH .gtoreq.12.5 (as 1% solns.) and **pKa** .gtoreq.11.5. Thus, bisphenol A epoxy resin 75, novolak phenolic resin 25, 1,5-azabicyclo(4.3.0)nonene-5 0.01, carnauba wax 63.9, and SiO2 190 parts were kneaded, crushed, and transfer molded with elements to give a test piece showing warpage 32 .mu.m after 6 h at 175.degree..

IT **3001-72-7**
RL: USES (Uses)
(epoxy resins contg., for sealants, for good warping resistance)

RN 3001-72-7 CAPLUS

CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:646758 CAPLUS
DOCUMENT NUMBER: 115:246758
TITLE: Preparation of indium alkoxides soluble in organic solvents
INVENTOR(S): Wettling, Danielle Marie Henriette; Moore, Christopher Peter
PATENT ASSIGNEE(S): Eastman Kodak Co., USA; Kodak-Pathe; Kodak Ltd.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

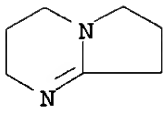
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9113848	A1	19910919	WO 1991-EP436	19910308
W: JP, US				
RW: DE, FR, GB, NL				
FR 2659649	A1	19910920	FR 1990-3646	19900316
FR 2659649	B1	19920612		
EP 519999	A1	19921230	EP 1991-906375	19910308
EP 519999	B1	19950614		
R: DE, FR, GB, NL				
JP 05504966	T2	19930729	JP 1991-505701	19910308
JP 2863630	B2	19990303		
US 5237081	A	19930817	US 1992-927524	19920915
PRIORITY APPLN. INFO.:			FR 1990-3646	19900316
			WO 1991-EP436	19910308

AB The prepn. consists in reacting an In halide with a C3-20 alc. in the presence of a base having a **pKa** >10 and a low nucleophilicity, in an anhyd. medium, under inert gas and in the presence of polar org. solvents. High-yield pure In alkoxides are obtained.

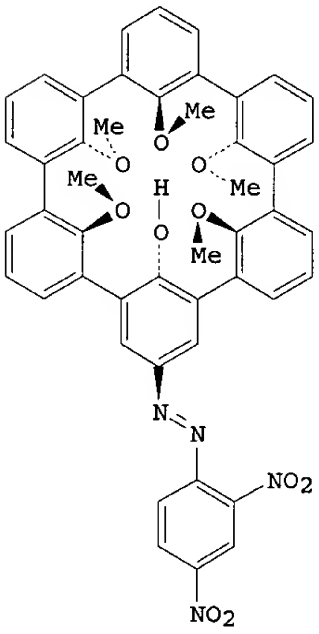
IT **3001-72-7**
RL: RCT (Reactant)
(base, in prepn. of indium alkoxide sol. in org. solvents)

RN 3001-72-7 CAPLUS

CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:44601 CAPLUS
DOCUMENT NUMBER: 108:44601
TITLE: Host-guest complexation. 45. A highly preorganized chromogenic spherand indicator system specific for sodium and lithium ions
AUTHOR(S): Cram, Donald J.; Carmack, Richard A.; Helgeson, Roger C.
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: J. Am. Chem. Soc. (1988), 110(2), 571-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

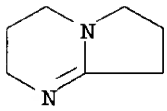


I

AB The synthesis and chromogenic properties of I as a Na and Li ion-selective indicator system are described. The **pKa** values of I in the absence and presence of various metal ions were measured in dioxane-20 vol% water as: Li+, 5.9; Na+, 6.9; K+, 12.7; Ca2+, 12.8; Mg2+, 13.2; 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 13.0. Spherand I is yellow (.lambda.max 396 nm; .epsilon.max 17500 L/(mol cm), whereas spheraplexes of I with Li+ (.lambda.max 586 nm, .epsilon.max 35500 L/(mol cm) and Na+ (.lambda.max 596 nm, .epsilon.max 35500 L/(mol.cm) as well as uncomplexed I- (.lambda.max 610 nm, .epsilon.max, 53000 L/(mol.cm) are deep blue or violet in dioxane-water mixt. and other solvents. Thus, I is a chromogenic ion-selective indicating system capable of detecting Li+ and Na+ at concns. as low as 10-8M in the presence of other, common ions.

IT **3001-72-7**, 1,5-Diazabicyclo[4.3.0]non-5-ene

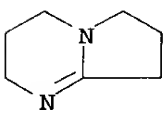
RL: PRP (Properties)
(anal. of lithium and sodium ions in presence of, chromogenic indicator for)
RN 3001-72-7 CAPLUS
CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:477313 CAPLUS
DOCUMENT NUMBER: 107:77313
TITLE: .alpha.-Hydroxyketones by condensation of aldehydes
INVENTOR(S): Beevor, Robert George
PATENT ASSIGNEE(S): British Petroleum Co. PLC, UK
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 219317	A1	19870422	EP 1986-307824	19861009
EP 219317	B1	19891123		
R: BE, DE, FR, GB, IT, NL, SE				
US 4782186	A	19881101	US 1986-911052	19860924
JP 62087543	A2	19870422	JP 1986-242871	19861013
JP 08032651	B4	19960329		

PRIORITY APPLN. INFO.: GB 1985-25402 19851015
AB .alpha.-Hydroxy ketones were prepd. by condensation of 1 or more aldehydes in the presence of a thiazolium salt and a sterically hindered base of **pKa** >12.0. A soln. of AcH, HCHO, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (I), and 3-ethylbenzothiazolium bromide in EtOH was heated at 60.degree. in a sealed tube with stirring for 1 h to give 43.5% conversion of AcH with selectivities of 91.0% to HOCH2COMe and 7.4% to 3-hydroxybutanone. Using NEt3 (**pKa** = 11) instead of I gave 24.9% conversion of AcH with selectivities of 84.5% to HOCH2COMe and 4.8% to 3-hydroxybutanone. The .alpha.-hydroxy ketones are useful as solvents, starting materials for org. synthesis, or as gasoline supplements.
IT **3001-72-7**, 1,5-Diazabicyclo[4.3.0]non-5-ene
RL: CAT (Catalyst use); USES (Uses)
(catalyst, for condensation of formaldehyde with acetaldehyde)
RN 3001-72-7 CAPLUS
CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:171656 CAPLUS

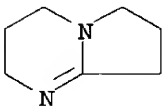
DOCUMENT NUMBER: 86:171656
TITLE: trans-Citral from cis-citral
INVENTOR(S): Ichikawa, Yataro; Yamamoto, Mamoru; Yamaji, Teizo
PATENT ASSIGNEE(S): Teijin, Ltd., Japan
SOURCE: Japan. Kokai, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 51133216	A2	19761118	JP 1975-55402	19750513
JP 58019652	B4	19830419		

AB Cis-citral isomerized to the trans isomer in the presence of a cyclic tertiary amine of **pKa** 7-13. Thus, cis-citral was heated with 10 mole % triethylenediamine in DMF at 200.degree. for 10 min to give trans-citral with 56.4% conversion and 97.5% selectivity. Similarly, N-methylpiperidine, quinuclidine, or 1,5-diazabicyclo[4.3.0]non-k-ene as catalyst gave 84-95% selectivity, vs. 10-35% with pyridine or Bu3N.

IT **3001-72-7**
RL: CAT (Catalyst use); USES (Uses)
(catalysts, for isomerization of cis-citral)

RN 3001-72-7 CAPLUS
CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



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=> d ibib abs hitstr 1-10 l17

L17 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:439114 CAPLUS
DOCUMENT NUMBER: 137:21064
TITLE: Polyamide compositions and multilayered plastics and tubes using them
INVENTOR(S): Arita, Hiroaki; Shimizu, Takumi
PATENT ASSIGNEE(S): Daicel-Degussa Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002167505	A2	20020611	JP 2000-366818	20001201

AB Title compns. comprise (A) polyamides with molar ratio of terminal CO2H groups to terminal NH2 groups >1, (B) aminocarboxylic acids with mol. wt. .ltoreq.15,000, and (C) bases or their salts with **pKa** (at 25.degree.) .gtoreq.10. The multilayered plastics and tubes comprise layers of the polyamides and fluoropolymer layers. The multilayered tubes are useful for fuel hoses of automobiles. Thus, a compn. contg. polyamide 12 (Daiamid), 12-aminododecanoic acid, 1,5-diazabicyclo[4.3.0]nonene-5 and THV 500 (hexafluoropropylene-tetrafluoroethylene-vinylidene fluoride copolymer) were extruded to give a multilayered tube with high 180.degree.-peel adhesion without over-reaction.

IT **3001-72-7**, DBN
RL: CAT (Catalyst use); USES (Uses)
(catalysts; polyamide compns. with good adhesion to fluoropolymers for multilayered tubes)

RN 3001-72-7 CAPLUS
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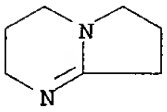

L17 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:403453 CAPLUS
DOCUMENT NUMBER: 135:19773
TITLE: Preparation of 3-(trialkylsiloxy)azetidines and their intermediates
INVENTOR(S): Tagata, Takeshi
PATENT ASSIGNEE(S): Koei Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001151784	A2	20010605	JP 1999-330478	19991119

OTHER SOURCE(S): CASREACT 135:19773; MARPAT 135:19773

=> d ibib abs hitstr 1-10 l17

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LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002167505	A2	20020611	JP 2000-366818	20001201

AB Title compns. comprise (A) polyamides with molar ratio of terminal CO2H groups to terminal NH2 groups >1, (B) aminocarboxylic acids with mol. wt. .ltoreq.15,000, and (C) bases or their salts with **pKa** (at 25.degree.) .gtoreq.10. The multilayered plastics and tubes comprise layers of the polyamides and fluoropolymer layers. The multilayered tubes are useful for fuel hoses of automobiles. Thus, a compn. contg. polyamide 12 (Daiamid), 12-aminododecanoic acid, 1,5-diazabicyclo[4.3.0]nonene-5 and THV 500 (hexafluoropropylene-tetrafluoroethylene-vinylidene fluoride copolymer) were extruded to give a multilayered tube with high 180.degree.-peel adhesion without over-reaction.

IT **3001-72-7**, DBN
RL: CAT (Catalyst use); USES (Uses)
(catalysts; polyamide compns. with good adhesion to fluoropolymers for multilayered tubes)

RN 3001-72-7 CAPLUS
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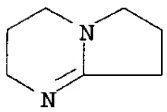

L17 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
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CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001151784	A2	20010605	JP 1999-330478	19991119

OTHER SOURCE(S): CASREACT 135:19773; MARPAT 135:19773

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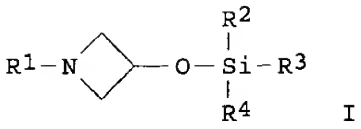


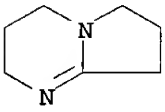
I

AB Title compds. I (R1 = alkyl, aralkyl; R2-R4 = alkyl) are prepd. by reaction of R1NHSiR2R3R4 (R1-R4 = same as I) with epihalohydrins in the presence of solid acid catalysts and cyclization of the resulting R1NHCH2CH(CH2X)OSiR2R3R4 (R1-R4 = same as I) in the presence of org. bases with **pKa** .gtoreq. 11. E.g., PhCH2NH2 was silylated by Me3SiCl in C6H6 in the presence of NEt3 at 0-10.degree. for 1 h, treated with epichlorohydrin in the presence of activated alumina at 22-25.degree. for 4 h, and cyclized using 1,5-diazabicyclo[4.3.0]nonene-5 in MeCN under reflux for 5.5 h to give 42% I (R1 = PhCH2, R2-R4 = Me).

IT **3001-72-7**, 1,5-Diazabicyclo[4.3.0]non-5-ene
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of (trialkylsiloxy)azetidines by cyclization of aminohalopropanes using org. bases)

RN 3001-72-7 CAPLUS

CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:69249 CAPLUS

DOCUMENT NUMBER: 134:132644

TITLE: Curable polyurethane foam compositions, manufacture of polyurethane foams, and sound insulators and seals for hard disks

INVENTOR(S): Kimura, Toshiaki; Sera, Noriyuki; Kusakawa, Koichi

PATENT ASSIGNEE(S): NHK Spring Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001026628	A2	20010130	JP 1999-200950	19990714

OTHER SOURCE(S): MARPAT 134:132644

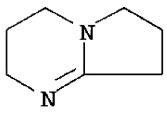
AB The compns., showing reduced gas generation, are manufd. by a reaction of polyols with polyfunctional isocyanates in the presence of catalysts comprising (A) reactive amines contg. .gtoreq.1 OH or SH and (B) amines having strong gelation effect and **pKa** .gtoreq.9. Thus, ethylene oxide-propylene oxide copolymer glycerin ether was polymd. and foamed with polypropylene glycol glycerin ether, triol crosslinking agent, 1,4-butanediol, and Isonate 143L (carbodiimide-modified MDI) in the presence of dimethylethanolamine, U-CAT SA 102 [1,8-diazabicyclo(5.4.0)-7-undecene], and H2O to give a foam, which when used as packing material

showed good airtightness.

IT **3001-72-7**, U-CAT 1102
RL: CAT (Catalyst use); USES (Uses)
(U-CAT 1102; manuf. of polyurethane foams for sound insulators and seals for hard disks)

RN 3001-72-7 CAPLUS

CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



L17 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:692356 CAPLUS

DOCUMENT NUMBER: 128:17348

TITLE: Chemical amplification positive-working resist composition containing nitrogen-containing organic compound

INVENTOR(S): Hatakeyama, Jun; Nagura, Shigehiro; Ishihara, Toshinobu

PATENT ASSIGNEE(S): Shin-Etsu Chemical Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

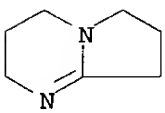
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09274312	A2	19971021	JP 1996-111309	19960408
JP 3125678	B2	20010122		

AB The material contains .gtoreq.1 of each N-contg. org. compds. (1) having **pKa** .gtoreq.7 and vapor pressure <2 and (2) having **pKa** .gtoreq.7 and vapor pressure 2-100 Torr at 100.degree.. The material comprises an org. solvent, a base resin, an acid-generating agent, and a mixt. of the above compds. The material shows high sensitivity toward high energy rays such as far UV rays, electron beams, and x-ray and provides high resoln. patterns with good profile by development with alk. aq. solns. Thus, poly(p-hydroxystyrene) of which the OH groups were partially protected with CH(OEt)Me group, p-tert-BuOC6H4S+Ph2.p-MeC6H4SO3-, 1,8-diazabicycloundecene, and quinoline were dissolved in propylene glycol monomethyl ether acetate to give a resist soln.

IT **3001-72-7**
RL: MOA (Modifier or additive use); TEM (Technical or engineered material use); USES (Uses)
(chem. amplification pos.-working resist contg. nitrogen-contg. org. compds.)

RN 3001-72-7 CAPLUS

CN Pyrrolo[1,2-a]pyrimidine, 2,3,4,6,7,8-hexahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)



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                   frequency
 NEWS  5  Feb 19   Access via Tymnet and SprintNet Eliminated Effective 3/31/02
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